INVENTOR SEARCH

=> d ibib abs ind l3 1-4

L3 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1059601 HCAPLUS Full-text
DOCUMENT NUMBER: 142:729
TITLE: In vitro platform for screening agents inducing **islet cell neogenesis**
INVENTOR(S): **Rosenberg, Lawrence**
PATENT ASSIGNEE(S): McGill University, Can.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004106921	A2	20041209	WO 2004-CA788	20040527
WO 2004106921	A3	20050609		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2567823	A1	20041209	CA 2004-2567823	20040527
EP 1631822	A2	20060308	EP 2004-734986	20040527
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007009882	A1	20070111	US 2005-558191	20051125

PRIORITY APPLN. INFO.:
US 2003-473153P P 20030527
WO 2004-CA788 W 20040527

AB The invention discloses an in vitro method for screening agents inducing **islet cell neogenesis** or duct-to-islet cell transdifferentiation, which comprises (a) expanding in vitro cells of a duct-like structure obtained by inducing cystic formation in cells in or associated with post-natal islets of Langerhans; (b) treating the expanded cells of said duct-like structure with an agent screened; and (c) determining potency of the agent of inducing islet cell differentiation of the duct-like structure in becoming insulin-producing cells.

IC ICM G01N033-50
ICS C12N005-06; C12Q001-68
CC 1-10 (Pharmacology)
Section cross-reference(s): 2, 13
ST **islet cell neogenesis** induction agent screening
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CK-19; in vitro platform for screening agents inducing **islet cell neogenesis**)
IT Culture media

(DMEM/F12; in vitro platform for screening agents inducing **islet cell neogenesis**)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IPF1 (insulin promoter factor 1); in vitro platform for screening agents inducing **islet cell neogenesis**)

IT Apoptosis
(anti-apoptotic agents; in vitro platform for screening agents inducing **islet cell neogenesis**)

IT Toxins
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cholera; in vitro platform for screening agents inducing **islet cell neogenesis**)

IT Pancreas
(duct, duct-to islet cell transdifferentiation; in vitro platform for screening agents inducing **islet cell neogenesis**)

IT Pancreas
(duct, epithelium; in vitro platform for screening agents inducing **islet cell neogenesis**)

IT Cell differentiation
(duct-to islet cell transdifferentiation; in vitro platform for screening agents inducing **islet cell neogenesis**)

IT Drug screening
Human
Immunosuppressants
Pancreatic islet of Langerhans
(in vitro platform for screening agents inducing **islet cell neogenesis**)

IT Growth factors, animal
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in vitro platform for screening agents inducing **islet cell neogenesis**)

IT Epithelium
(pancreatic ductal; in vitro platform for screening agents inducing **islet cell neogenesis**)

IT Collagens, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(type I; in vitro platform for screening agents inducing **islet cell neogenesis**)

IT 9004-10-8, Insulin, biological studies 9007-92-5, Glucagon, biological studies 51110-01-1, Somatostatin 148640-14-6, Akt kinase 155215-87-5, Jnk kinase 169592-56-7, Caspase 3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro platform for screening agents inducing **islet cell neogenesis**)

IT 62229-50-9, EGF
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in vitro platform for screening agents inducing **islet cell neogenesis**)

IT 151820-83-6, Ilotropin
RL: PAC (Pharmacological activity); BIOL (Biological study)
(in vitro platform for screening agents inducing **islet cell neogenesis**)

L3 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:368941 HCAPLUS Full-text
DOCUMENT NUMBER: 140:368703
TITLE: Methods and composition using INGAP peptides and other pro-**neogenesis** factors for reversal of diabetes
INVENTOR(S): **Rosenberg, Lawrence**
PATENT ASSIGNEE(S): McGill University, Can.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037277	A2	20040506	WO 2003-CA1635	20031024
WO 2004037277	A3	20040715		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003275853	A1	20040513	AU 2003-275853	20031024
US 2006009516	A1	20060112	US 2005-532426	20050422
PRIORITY APPLN. INFO.:			US 2002-420677P P	20021024
			WO 2003-CA1635 W	20031024

AB The invention relates to a method to stimulate reversal of a diabetic state in a patient; a method to prevent autoimmune destruction of new insulin-producing cells (pancreatic β-cells) in a patient; a method to promote survival of the newly regenerated insulin-producing cells (pancreatic β-cells); and an in vivo method for the induction of **islet cell neogenesis** and new islet formation and the prevention of autoimmune destruction of the new cells. The methodol. of the invention uses INGAP peptides and other pro- **neogenesis** factors.

IC ICM A61K038-00
CC 1-10 (Pharmacology)
Section cross-reference(s): 63
ST diabetes reversal INGAP peptide **neogenesis** factor; pancreas beta cell INGAP peptide **neogenesis** factor; **islet cell neogenesis** diabetes reversal
IT Antidiabetic agents
Autoimmune disease
Diabetes mellitus
Drug delivery systems
Drug interactions
Human
Immunosuppressants
Pancreas
Pancreatic islet of Langerhans
(INGAP peptides and other pro-**neogenesis** factors for reversal of diabetes)
IT Growth factors, animal
Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(INGAP peptides and other pro-**neogenesis** factors for reversal of diabetes)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(islet **neogenesis**-associated protein (INGAP), fragments; INGAP peptides and other pro-**neogenesis** factors for reversal of diabetes)

IT Stem cell
(islet; INGAP peptides and other pro-**neogenesis** factors for reversal of diabetes)

IT Pancreatic islet of Langerhans
(β-cell; INGAP peptides and other pro-**neogenesis** factors for reversal of diabetes)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(INGAP peptides and other pro-**neogenesis** factors for reversal of diabetes)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(INGAP peptides and other pro-**neogenesis** factors for reversal of diabetes)

IT 9002-76-0, Gastrin 9061-61-4, Nerve growth factor 53123-88-9, Sirolimus 62229-50-9, Epidermal growth factor 67763-96-6, IGF-I 67763-97-7, IGF-II 89750-14-1, GLP-1 104987-11-3, Tacrolimus 141732-76-5, Exendin 4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(INGAP peptides and other pro-**neogenesis** factors for reversal of diabetes)

IT 685158-34-3
RL: PRP (Properties)
(unclaimed protein sequence; methods and composition using INGAP peptides and other pro-**neogenesis** factors for reversal of diabetes)

IT 457632-26-7
RL: PRP (Properties)
(unclaimed sequence; methods and composition using INGAP peptides and other pro-**neogenesis** factors for reversal of diabetes)

L3 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:320123 HCAPLUS Full-text
DOCUMENT NUMBER: 138:331711
TITLE: Use of **islet cell neogenesis** associated protein for treatment of diabetes
INVENTOR(S): Vinik, Aaron I.; **Rosenberg, Lawrence**; Pittenger, Gary; Taylor-Fishwick, David; Salem, Michael; Mohrland, Scott
PATENT ASSIGNEE(S): The Procter & Gamble Company, USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003033808	A2	20030424	WO 2002-US32904	20021015

WO 2003033808 A3 20030918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004132644	A1	20040708	US 2002-253733		20020924
CA 2463769	A1	20030424	CA 2002-2463769		20021015
AU 2002343519	A1	20030428	AU 2002-343519		20021015
EP 1435995	A2	20040714	EP 2002-780465		20021015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002013291	A	20041026	BR 2002-13291		20021015
HU 200401612	A2	20041228	HU 2004-1612		20021015
JP 2005506362	T	20050303	JP 2003-536523		20021015
CN 1723034	A	20060118	CN 2002-820192		20021015
ZA 2004002261	A	20040928	ZA 2004-2261		20040323
IN 2004DN00768	A	20060721	IN 2004-DN768		20040324
MX 2004PA03526	A	20040722	MX 2004-PA3526		20040415
NO 2004002012	A	20040716	NO 2004-2012		20040514
IN 2004DN03585	A	20050401	IN 2004-DN3585		20041116
PRIORITY APPLN. INFO.:			US 2001-329330P	P	20011016
			WO 2002-US32904	W	20021015

AB The present invention comprises dosing regimens and formulations of **islet cell neogenesis** associated protein (INGAP) and INGAP Peptide. The formulation disclosed herein is shown have acceptable stability as a pharmaceutical composition Further, the formulation is able to regenerate functional islets.

IC ICM D06M

CC 1-10 (Pharmacology)
Section cross-reference(s): 3, 6, 14

ST cell **neogenesis** assocd protein treatment diabetes; INGAP Peptide sequence human

IT Peptides, biological studies
Proteins
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(INGAP (**islet cell neogenesis** associated protein); use of **islet cell neogenesis** associated protein for treatment of diabetes)

IT Drug delivery systems
Test kits
(INGAP peptide in; use of **islet cell neogenesis** associated protein for treatment of diabetes)

IT Canis familiaris
Hamster
Mus
(as disease model for diabetes; use of **islet cell neogenesis** associated protein for treatment of diabetes)

IT Disease models
(for diabetes, hamster, dog, mouse; use of **islet cell neogenesis** associated protein for treatment of diabetes)

IT Pancreatic islet of Langerhans
(**neogenesis**, INGAP peptide in; use of **islet cell neogenesis** associated protein for treatment of diabetes)

IT Protein sequences
(of INGAP of human; use of **islet cell neogenesis** associated protein for treatment of diabetes)
IT pH
(of INGAP peptide in drug delivery system; use of **islet cell neogenesis** associated protein for treatment of diabetes)
IT Antidiabetic agents
Diabetes mellitus
Human
Mammalia
(use of **islet cell neogenesis** associated protein for treatment of diabetes)
IT Pancreatic islet of Langerhans
(β-cell, **neogenesis**, INGAP peptide in; use of **islet cell neogenesis** associated protein for treatment of diabetes)
IT 353273-97-9 515814-91-2
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(INGAP peptide sequence; use of **islet cell neogenesis** associated protein for treatment of diabetes)
IT 515888-30-9
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; use of **islet cell neogenesis** associated protein for treatment of diabetes)
IT 50-99-7, Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(regulation, INGAP peptide in; use of **islet cell neogenesis** associated protein for treatment of diabetes)

L3 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:815901 HCAPLUS Full-text
DOCUMENT NUMBER: 130:180535
TITLE: Induction of **islet cell neogenesis** in the adult pancreas: The partial duct obstruction model
AUTHOR(S): **Rosenberg, Lawrence**
CORPORATE SOURCE: Montreal General Hospital, Montreal, QC, H3G 1A4, Can.
SOURCE: Microscopy Research and Technique (1998), 43(4), 337-346
CODEN: MRTEEO; ISSN: 1059-910X
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The proliferative capacity of adult pancreatic islet cells is limited, although the formation of new islets from cells associated with the ductal epithelium is achievable even in the adult gland. Understanding the mechanism whereby proliferation and subsequent differentiation of putative precursor cells leads the appearance of new islets, i.e., islet **neogenesis**, may be important as a modality for treatment of both Type I and type II diabetes, in which there is an absolute or relative deficiency of insulin. It appears that certain genes and their protein products are essential to the initiation of the initial step in the pathway. We have shown that partial obstruction of the hamster pancreas is able to reverse streptozotocin-induced diabetes more than 50% of the time. An extract, termed ilotropin, prepared from obstructed pancreas, also reverses the diabetes, whereas exts. of control non-obstructed pancreas do not. Ilotropin contains a protein that is heat and acid stable with MW around 20-45 kDa that is capable of stimulating the proliferation of

isolated duct cells in culture. Using mRNA and a differential display technique, 20 genes were found to be expressed in the partially obstructed (regenerating), but not the non-obstructed (non-regenerating) pancreas. One of these islet **neogenesis**-associated proteins (INGAP) proved to be unique to the obstructed pancreas, and a peptide contained within the sequence was capable of stimulating the proliferation of ductal cells in culture. INGAP was found to be expressed early in the neogenic process before the onset of ductal cell proliferation, and was capable of stimulating tritiated thymidine uptake into protodifferentiated epithelial cells, compatible with the notion that it might be involved in initiating the process of islet **neogenesis**.

CC 13-6 (Mammalian Biochemistry)

ST ilotropin pancreas islet cell regeneration diabetes

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(INGAP (islet **neogenesis**-associated protein); induction of **islet cell neogenesis** in adult pancreas - partial duct obstruction model)

IT Pancreas
(duct cell; induction of **islet cell neogenesis** in adult pancreas - partial duct obstruction model)

IT Pancreas
Regeneration, animal
(induction of **islet cell neogenesis** in adult pancreas - partial duct obstruction model)

IT Diabetes mellitus
(insulin-dependent; induction of **islet cell neogenesis** in adult pancreas - partial duct obstruction model)

IT Diabetes mellitus
(non-insulin-dependent; induction of **islet cell neogenesis** in adult pancreas - partial duct obstruction model)

IT Pancreatic islet of Langerhans
(β-cell; induction of **islet cell neogenesis** in adult pancreas - partial duct obstruction model)

IT 151820-83-6, Ilotropin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(induction of **islet cell neogenesis** in adult pancreas - partial duct obstruction model)

IT 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(induction of **islet cell neogenesis** in adult pancreas - partial duct obstruction model)

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RESULTS FROM REGISTRY, CAPLUS, AND USPATFULL

```
=> d que stat l31
L5            1 SEA FILE=REGISTRY ABB=ON  "DMEM/F 12"/CN
L6        25766 SEA FILE=HCAPLUS ABB=ON  ?PANCREATIC?(W)?ISLET?(3W)?LANGERHANS?
                  OR ?ISLET?(W)?CELL?
L7         2869 SEA FILE=HCAPLUS ABB=ON  L6 AND ?TRANSCRIPT?
L8          403 SEA FILE=HCAPLUS ABB=ON  L7 AND ?VITRO?
L9          127 SEA FILE=HCAPLUS ABB=ON  L8 AND ?CELL?(W)?DIFFER?
L10          67 SEA FILE=HCAPLUS ABB=ON  L9 AND ?DUCT?
L11          14 SEA FILE=HCAPLUS ABB=ON  L9 AND ?DUCT?(4A)?ISLET?
L13          67 SEA FILE=HCAPLUS ABB=ON  L10 OR L11
L15          23 SEA FILE=HCAPLUS ABB=ON  L13 AND ?GROWTH?(W)?FACTOR?
L18           4 SEA FILE=HCAPLUS ABB=ON  L13 AND (L5 OR DMEM)
L19           4 SEA FILE=HCAPLUS ABB=ON  L13 AND (L5 OR DMEM?)
L20          24 SEA FILE=HCAPLUS ABB=ON  L15 OR L18 OR L19
L21           7 SEA FILE=HCAPLUS ABB=ON  L20 AND (EGF OR ?CHOLERA?(W)?TOXIN?)
L22          24 SEA FILE=HCAPLUS ABB=ON  L20 OR L21
L23          15 SEA FILE=HCAPLUS ABB=ON  L22 AND ?HUMAN?
L24          24 SEA FILE=HCAPLUS ABB=ON  L22 OR L23
L25          21 SEA FILE=HCAPLUS ABB=ON  L24 AND (PRD<20051125 OR PD<20051125)

L26        1841 SEA FILE=USPATFULL ABB=ON  L24 AND (PRD<20051125 OR PD<20051125
                  )
L27        1568 SEA FILE=USPATFULL ABB=ON  L26 AND ?COLLAGEN?
L28         106 SEA FILE=USPATFULL ABB=ON  L27 AND GEL(W)?MATRIX?
L29          82 SEA FILE=USPATFULL ABB=ON  L28 AND (L5 OR DMEM)
L30           7 SEA FILE=USPATFULL ABB=ON  L29 AND ?CHOLERA?(W)?TOXIN?
L31          28 DUP REMOV L25 L30 (0 DUPLICATES REMOVED)


=> d ibib abs l31 1-28

L31  ANSWER 1 OF 28  USPATFULL on STN
ACCESSION NUMBER:        2007:11473  USPATFULL  Full-text
TITLE:                   In vitro platform for screening agents
                         inducing islet cell neogenesis
INVENTOR(S):             Rosenberg, Lawrence, Montreal, CANADA
PATENT ASSIGNEE(S):      McGill University, Montreal, QC, CANADA, H3A 3L8
                         (non-U.S. corporation)

                              NUMBER         KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2007009882      A1   20070111
APPLICATION INFO.:       US 2004-558191     A1   20040527  (10)
                         WO 2004-CA788           20040527
                                                 20051125  PCT 371 date

                                NUMBER         DATE
                         ------------------- --------
PRIORITY INFORMATION:    US 2003-473153P     20030527 (60)          <--
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    BERESKIN AND PARR, 40 KING STREET WEST, BOX 401,
                         TORONTO, ON, M5H 3Y2, CA
NUMBER OF CLAIMS:        12
EXEMPLARY CLAIM:         1
NUMBER OF DRAWINGS:      10 Drawing Page(s)
LINE COUNT:              579
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to an in **vitro** method for screening agents inducing **islet cell** neogenesis or **duct**-to-**islet cell transdifferentiation**, which comprises the steps of: a) expanding in **vitro** cells of a **duct**-like structure obtained by inducing cystic formation in cells in or associated with post-natal islets of Langerhans; b) treating said expanded cells of said **duct**-like structure with an agent screened; and c) determining potency of said agent of inducing **islet cell differentiation** of said **duct**-like structure in becoming insulin-producing cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L31 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1157631 HCAPLUS Full-text
DOCUMENT NUMBER: 145:483673
TITLE: Novel methods and devices for evaluating poisons
INVENTOR(S): Ching, Edwin P.; Johnson, Dale E.; Sudarsanam, Sucha
PATENT ASSIGNEE(S): Emiliem, USA
SOURCE: PCT Int. Appl., 132pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006116622	A2	20061102	WO 2006-US16067	20060426 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006253262	A1	20061109	US 2006-380388	20060426 <--
PRIORITY APPLN. INFO.:			US 2005-675741P	P 20050427 <--
			US 2006-778133P	P 20060301

AB Methods and devices useful for evaluating poisons or other chemical entities, and for using such methods to forecast unfavorable drug effects. The present invention provides lists of biomarkers for anal., either directly or indirectly, which affect the toxicity pathways. These may be evaluated at many levels, including genetic, genotyping, evaluation of combination pairing of diploid alleles or haplotypes, RNA expression, protein expression, functional activity, posttranslational anal. or evaluation, etc. Thus, the biomarkers refer to the corresponding genetic information, RNA, protein, or other structural embodiments thereof. And the means to use these biomarkers, e.g., to evaluate status of toxicity pathways, to evaluate individual risk or susceptibility to various toxic pathways from exposure or therapeutic intervention, to generate test systems for drug development, are all provided by identifying critical and significant contributors to the pathway progression. The present invention is directed to accelerating the speed of development and reducing the resource investment necessary to determine these

features for directing use of such substances or treatments to appropriate biol. contexts.

L31 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:885851 HCAPLUS Full-text
DOCUMENT NUMBER: 145:288120
TITLE: Isolation, culture and therapeutic use of **human** trophoblast stem cells
INVENTOR(S): Lee, Jau-Nan; Lee, Tony Tung-Ying; Lee, Yuta
PATENT ASSIGNEE(S): Taiwan
SOURCE: PCT Int. Appl., 65pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006091766	A2	20060831	WO 2006-US6512	20060224 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006211110	A1	20060921	US 2006-361588	20060224 <--
PRIORITY APPLN. INFO.:			US 2005-655747P	P 20050224 <--

AB Existence of **human** trophoblast stem (hTS) cells has been suspected but unproved. The isolation of hTS cells is reported at the early stage of chorionic villi by expression of FGF4, fgfr-2, Oct4, Thy-1, and stage-specific embryonic antigens distributed in different compartments of the cell. HTS cells are able to derive into specific cell phenotypes of the three primitive embryonic layers, produce chimeric reactions in mice, and retain a normal karyotype and telomere length. In hTS cells, Oct4 and fgfr-2 expression can be knocked down by bFGF. These facts suggest that differentiation of the hTS cells play an important role in implantation and placentation. HTS cells could be applied to **human cell differentiation** and for gene- and cell-based therapies.

L31 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:656853 HCAPLUS Full-text
DOCUMENT NUMBER: 145:120042
TITLE: Isolation, characterization and therapeutic use of postpartum cells derived from **human** umbilical cord tissue
INVENTOR(S): Harris, Ian Ross; Messina, Darin J.; Kihm, Anthony; Seyda, Agneiszka; Colter, David
PATENT ASSIGNEE(S): Ethicon Incorporated, USA
SOURCE: PCT Int. Appl., 185 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006071794	A2	20060706	WO 2005-US46851	20051222 <--
WO 2006071794	A3	20070125		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005322060	A1	20060706	AU 2005-322060	20051222 <--
CA 2589041	A1	20060706	CA 2005-2589041	20051222 <--
EP 1831356	A2	20070912	EP 2005-855417	20051222 <--
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: US 2004-639088P P 20041223 <--
WO 2005-US46851 W 20051222

AB Cells derived from **human** umbilical cords are disclosed along with methods for their therapeutic use, e.g., transplantation. Isolation techniques, culture methods and detailed characterization of the cells with respect to their cell surface markers, gene expression, and their secretion of trophic factors are described.

L31 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1041273 HCAPLUS Full-text
DOCUMENT NUMBER: 145:372371
TITLE: Culture methods, characterization and therapeutic use of postpartum cells derived from umbilical cord
INVENTOR(S): Harris, Ian Ross; Messina, Darin J.; Kihm, Anthony J.; Seyda, Agnieszka; Colter, David C.
PATENT ASSIGNEE(S): Ethicon Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 81pp., Cont.-in-part of U.S. Ser. No. 877,012.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006223177	A1	20061005	US 2005-315897	20051222 <--
US 2005054098	A1	20050310	US 2004-877012	20040625 <--
AU 2004281371	A1	20050428	AU 2004-281371	20040625 <--
CA 2530412	A1	20050428	CA 2004-2530412	20040625 <--
EP 1649013	A2	20060426	EP 2004-809466	20040625 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
US 2006234376	A1	20061019	US 2005-317574	20051223 <--

US 2006188983	A1	20060824	US 2005-322372		20051230 <--
US 2007009494	A1	20070111	US 2006-481480		20060706 <--
US 2007014771	A1	20070118	US 2006-481481		20060706 <--
US 2007036767	A1	20070215	US 2006-481456		20060706 <--
PRIORITY APPLN. INFO.:			US 2003-483264P	P	20030627 <--
			US 2004-877012	A2	20040625 <--
			US 2004-639088P	P	20041223 <--
			US 2004-877445	A3	20040625 <--
			US 2004-877541	A3	20040625 <--
			WO 2004-US20958	W	20040625 <--

AB Cells derived from **human** umbilical cords are disclosed along with methods for their therapeutic use, e.g., transplantation. Isolation techniques, culture methods and detailed characterization of the cells with respect to their cell surface markers, gene expression, and their secretion of trophic factors are described.

L31 ANSWER 6 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2006:261121 USPATFULL Full-text
TITLE: Amnion-derived cell compositions, methods of making and uses thereof
INVENTOR(S): Clarke, Diana L., Pittsburgh, PA, UNITED STATES
Smith, Charlotte A., Pittsburgh, PA, UNITED STATES
Banas, Richard A., Turtle Creek, PA, UNITED STATES
Marshall, Vivienne S., Glenshaw, PA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006222634	A1	20061005	
APPLICATION INFO.:	US 2006-392892	A1	20060329	(11)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2005-666949P	20050331 (60)	<--
	US 2005-699257P	20050714 (60)	<--
	US 2005-742067P	20051202 (60)	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LINDA O. PALLADINO, 45 HONEYSUCKLE COURT, STORMVILLE, NY, 12582, US
NUMBER OF CLAIMS: 55
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 4496
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is directed to substantially purified amnion-derived cell populations, compositions comprising the substantially purified amnion-derived cell populations, and to methods of creating such substantially purified amnion-derived cell populations, as well as methods of use. The invention is further directed to antibodies, in particular, monoclonal antibodies, that bind to amnion-derived cells or, alternatively, to one or more amnion-derived cell surface protein markers. The invention is further directed to methods for producing the antibodies, methods for using the antibodies, and kits comprising the antibodies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L31 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1103869 HCAPLUS Full-text

DOCUMENT NUMBER: 143:362858
TITLE: Pancreatic precursor cell line transdifferentiated from pancreatic acinar cell
INVENTOR(S): Song, Si-Young; Lee, Ji-Eun; Kim, Han-Soo; Wen, Jing
PATENT ASSIGNEE(S): Yonsei University, S. Korea
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005095589	A1	20051013	WO 2004-KR2669	20041018 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2005097619	A	20051010	KR 2004-22791	20040402 <--
PRIORITY APPLN. INFO.:			KR 2004-22791 A	20040402 <--

AB Disclosed are pancreatic precursor **cells transdifferentiated** from pancreatic acinar cells, which express both a pancreatic **ductal** cell marker gene and a gene participating in the pancreatic development, and a method of preparing such pancreatic precursor cells, comprising (1) isolating the pancreatic acinar cells from an adult, (2) in **vitro** culturing of the pancreatic acinar cells in a medium for mammalian cell culture and (3) isolating the pancreatic precursor cells expressing both a pancreatic **ductal** cell marker gene and a gene participating in the pancreatic development during the in **vitro** culturing. In addition, the present invention discloses pancreatic **islet cells** that are transdifferentiated from the pancreatic precursor cells and express a pancreatic **islet cell** marker gene, and a method of preparing such pancreatic **islet cells**, comprising (1) contacting the pancreatic precursor cells, prepared as described above, with a **growth factor**, (2) culturing the pancreatic precursor cells in a medium for mammalian cell culture and (3) isolating the pancreatic **islet cells** expressing a pancreatic **islet cell** marker gene during the culturing.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:34885 HCAPLUS Full-text
DOCUMENT NUMBER: 142:130333
TITLE: Isolation, culture, characterization and therapeutic use of postpartum cells derived from **human** umbilical cord
INVENTOR(S): Mistry, Sanjay; Kihm, Anthony J.; Harris, Ian Ross; Harmon, Alexander M.; Messina, Darin J.; Seyda, Agnieszka; Yi, Chin-Feng; Gosiewska, Anna
PATENT ASSIGNEE(S): Ethicon, Incorporated, USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003334	A2	20050113	WO 2004-US20931	20040625 <--
WO 2005003334	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004254616	A1	20050113	AU 2004-254616	20040625 <--
CA 2530533	A1	20050113	CA 2004-2530533	20040625 <--
US 2005037491	A1	20050217	US 2004-877541	20040625 <--
US 2005058630	A1	20050317	US 2004-877445	20040625 <--
US 2005058631	A1	20050317	US 2004-877446	20040625 <--
AU 2004281371	A1	20050428	AU 2004-281371	20040625 <--
CA 2530412	A1	20050428	CA 2004-2530412	20040625 <--
WO 2005038012	A2	20050428	WO 2004-US20958	20040625 <--
WO 2005038012	A3	20050915		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1641913	A2	20060405	EP 2004-756395	20040625 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
EP 1649013	A2	20060426	EP 2004-809466	20040625 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007521008	T	20070802	JP 2006-517783	20040625 <--
US 2006234376	A1	20061019	US 2005-317574	20051223 <--
US 2006188983	A1	20060824	US 2005-322372	20051230 <--
PRIORITY APPLN. INFO.:			US 2003-483264P	P 20030627 <--
			US 2004-877445	A3 20040625 <--
			US 2004-877541	A3 20040625 <--
			WO 2004-US20931	W 20040625 <--
			WO 2004-US20958	W 20040625 <--

AB Cells derived from **human** umbilical cords are disclosed along with methods for their therapeutic use (such as transplantation). Isolation techniques, culture methods and detailed characterization of the cells with respect to their cell surface markers, gene expression, and their secretion of trophic factors are described.

L31 ANSWER 9 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2005:274539 USPATFULL Full-text
TITLE: Use of Pin1 inhibitors for treatment of cancer
INVENTOR(S): Lu, Kun Ping, Newton, MA, UNITED STATES
Sowadski, Janusz M., Boston, MA, UNITED STATES
PATENT ASSIGNEE(S): BETH ISRAEL DEACONESS MEDICAL CENTER, Boston, MA, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005239095	A1	20051027	<--
APPLICATION INFO.:	US 2004-946445	A1	20040920 (10)	

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-504117P	20030919 (60)	<--
	US 2004-580814P	20040618 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LAHIVE & COCKFIELD, LLP., 28 STATE STREET, BOSTON, MA, 02109, US
NUMBER OF CLAIMS: 66
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Page(s)
LINE COUNT: 2912
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The instant invention provides methods for determining if a subject will benefit from treatment with a Pin1 modulator based on the expression of Pin1 and one or more cancer associated polypeptides, e.g., her2/neu, ras, cyclin D1, Cdk4, E2F, Myc, Jun, and Rb. The invention further provides methods for determining if a subject will benefit from treatment with one or more cancer treatments, alone or in combination with a Pin1 modulator.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L31 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1159809 HCAPLUS Full-text
DOCUMENT NUMBER: 144:32483
TITLE: Betacellulin-δ4, a novel differentiation factor for pancreatic β-cells, ameliorates glucose intolerance in streptozotocin-treated rats
AUTHOR(S): Ogata, Takeki; Dunbar, Andrew J.; Yamamoto, Yoritsuna; Tanaka, Yuji; Seno, Masaharu; Kojima, Itaru
CORPORATE SOURCE: Institute for Molecular and Cellular Regulation, Gunma University, Maebashi, 371-8512, Japan
SOURCE: Endocrinology (**2005**), 146(11), 4673-4681
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors previously described a novel alternatively spliced mRNA **transcript** of the betacellulin (BTC) gene. This splice isoform, termed BTC-δ4, lacks the C-loop of the epidermal **growth factor** motif and the transmembrane domain as a result of exon 4' skipping'. In this study, the authors expressed BTC-δ4 recombinantly to explore its biol. function. When BTC-δ4 was expressed in COS-7 cells, it was secreted largely into the culture medium, in contrast to BTC. Unlike BTC, highly purified recombinant BTC-δ4 produced in Escherichia coli failed to bind or induce tyrosine phosphorylation of either ErbB1 or

ErbB4, nor did it antagonize the binding of BTC to these receptors. Consistent with this, BTC-δ4 failed to stimulate DNA synthesis in Balb/c 3T3 and INS-1 cells. However, BTC-δ4 induced differentiation of pancreatic β-cells; BTC-δ4 converted AR42J cells to insulin-producing cells. When recombinant BTC-δ4 was administered to streptozotocin-treated neonatal rats, it reduced the plasma glucose concentration and improved glucose tolerance. Importantly, BTC-δ4 significantly increased the insulin content, the β-cell mass, and the nos. of islet-like cell clusters and PDX-1-pos. **ductal** cells. Thus, BTC-δ4 is a secreted protein that stimulates differentiation of β-cells in **vitro** and in vivo in an apparent ErbB1- and ErbB4-independent manner. The mechanism by which BTC-δ4 exerts this action on β-cells remains to be defined but presumably involves an, as yet, unidentified unique receptor.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:494650 HCAPLUS Full-text
DOCUMENT NUMBER: 143:110140
TITLE: Combination therapy with epidermal **growth factor** and gastrin induces neogenesis of **human islet** β-cells from pancreatic **duct** cells and an increase in functional β-cell mass
AUTHOR(S): Suarez-Pinzon, Wilma L.; Lakey, Jonathan R. T.; Brand, Stephen J.; Rabinovitch, Alex
CORPORATE SOURCE: Department of Medicine, University of Alberta, Edmonton, T6G 2S2, Can.
SOURCE: Journal of Clinical Endocrinology and Metabolism (**2005**), 90(6), 3401-3409
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pancreatic islet transplantation is a viable treatment for type 1 diabetes, but is limited by **human** donor tissue availability. The combination of epidermal **growth factor** (**EGF**) and gastrin induces islet β-cell neogenesis from pancreatic exocrine **duct** cells in rodents. In this study we investigated whether **EGF** and gastrin could expand the β-cell mass in adult **human** isolated **islets** that contain **duct** as well as endocrine cells. **Human islet cells** were cultured for 4 wk in serum-free medium (control) or in medium with **EGF** (0.3 μg/mL), gastrin (1.0 μg/mL), or the combination of **EGF** and gastrin. β-Cell nos. were increased in cultures with **EGF** plus gastrin (+118%) and with **EGF** (+81%), but not in cultures with gastrin (-3%) or control medium (-62%). After withdrawal of **EGF** and gastrin and an addnl. 4 wk in control medium, β-cell nos. continued to increase only in cultures previously incubated with both **EGF** and gastrin (+232%). **EGF** plus gastrin also significantly increased cytokeratin 19-pos. **duct** cells (+678%) in the cultures. Gastrin, alone or in combination with **EGF**, but not **EGF** alone, increased the expression of pancreatic and duodenal homeobox factor-1 as well as insulin and C peptide in the cytokeratin 19-pos. **duct** cells. Also, **EGF** plus gastrin significantly increased β-cells and insulin content in **human** islets implanted in immunodeficient nonobese diabetic-severe combined immune deficiency mice as well as insulin secretory responses of the **human** islet grafts to glucose challenge. In conclusion, combination therapy with **EGF** and gastrin increases β-cell mass in adult **human** pancreatic islets in **vitro** and in vivo, and this appears to result from the **induction** of β-cell neogenesis from pancreatic exocrine **duct** cells.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:558280 HCAPLUS Full-text
DOCUMENT NUMBER: 144:20048
TITLE: Nestin-positive progenitor cells isolated from **human** fetal pancreas have phenotypic markers identical to mesenchymal stem cells
AUTHOR(S): Zhang, Ling; Hong, Tian-Pei; Hu, Jiang; Liu, Yi-Nan; Wu, Yong-Hua; Li, Ling-Song
CORPORATE SOURCE: Department of Endocrinology, Peking University Third Hospital, Beijing, 100083, Peop. Rep. China
SOURCE: World Journal of Gastroenterology (**2005**), 11(19), 2906-2911
CODEN: WJGAF2; ISSN: 1007-9327
PUBLISHER: World Journal of Gastroenterology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Aim: To isolate nestin-pos. progenitor cells from **human** fetal pancreas and to detect their surface markers and their capability of proliferation and differentiation into pancreatic islet endocrine cells in **vitro**. Methods: Islet-like cell clusters (ICCs) were isolated from **human** fetal pancreas by using collagenase digestion. The free-floating ICCs were handpicked and cultured in a new dish. After the ICCs developed into monolayer epithelium-like cells, they were passaged and induced for differentiation. Reverse **transcription** polymerase chain reaction (RT-PCR), immunofluorescence stain, fluorescence-activated cell sorting (FACS) and RIA (RIA) were used to detect the expression of cell markers. Results:. (1) The monolayer epithelium-like cells had highly proliferative potential and could be passaged more than 16 times in **vitro**;. (2) RT-PCR anal. and immunofluorescence stain showed that these cells expressed both nestin and ABCG2, two of stem cell markers;. (3) FACS anal. revealed that CD44, CD90 and CD147 were pos., whereas CD34, CD38, CD45, CD71, CD117, CD133 and HLA-DR were neg. on the nestin-pos. cells;. (4) RT-PCR anal. showed that the mRNA expression of insulin, glucagon and pancreaticduodenal homeobox gene-1 was detected, whereas the expression of nestin and neurogenin 3 disappeared in these cells treated with serum-free media supplemented with the cocktail of **growth factors**. Furthermore, the intracellular insulin content was detected by RIA after the **induction** culture. Conclusion: Nestin-pos. cells isolated from **human** fetal pancreas possess the characteristics of pancreatic progenitor cells since they have highly proliferative potential and the capability of differentiation into insulin-producing cells in **vitro**. Interestingly, the nestin-pos. pancreatic progenitor cells share many phenotypic markers with mesenchymal stem cells derived from bone marrow.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:986380 HCAPLUS Full-text
DOCUMENT NUMBER: 143:383743
TITLE: Metaplasia in the pancreas
AUTHOR(S): Lardon, Jessy; Bouwens, Luc
CORPORATE SOURCE: Cell Differentiation Unit, Diabetes Research Center, Free University of Brussels-Vrije Universiteit Brussel, Brussels, B-1090, Belg.
SOURCE: Differentiation (Malden, MA, United States) (**2005**), 73(6), 278-286
CODEN: DFFNAW; ISSN: 0301-4681
PUBLISHER: Blackwell Publishing, Inc.

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. There is currently much interest in the possibility to treat chronic diseases by cell replacement or regenerative therapies. Most of these studies focus on the manipulation of undifferentiated stem cells. However, tissue repair and regeneration can also be achieved by differentiated cells, which, in certain conditions, can even transdifferentiate to other cell types. Such transdifferentiations can lead to tissue metaplasia. The pancreas is an organ wherein metaplasia was well investigated and for which exptl. models were recently developed allowing to unravel the mol. basis of transdifferentiation. Pancreatic metaplasias studied so far include the conversion of exocrine acinar cells to **duct** cells, exocrine cells to endocrine **islet cells**, endocrine cells to **duct** cells, and acinar cells to hepatocytes. Epitheliomesenchymal transitions were also described. The available evidence indicates that mature cells can be reprogrammed by specific environmental cues inducing the expression of cell type-specific **transcription** factors. For example, the glucocorticoid hormone dexamethasone induces pancreatic transdifferentiation to hepatocytes, whereas the combination of epidermal **growth factor** and leukemia-inhibitory factor induces exocrine-endocrine transdifferentiation in **vitro**. Further unravelling of the involved signal **transduction** pathways, **transcription** factor networks, and chromatin modifications is required to manipulate metaplasia at will and to apply it in tissue repair or regeneration.

REFERENCE COUNT: 111 THERE ARE 111 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:927163 HCAPLUS Full-text
DOCUMENT NUMBER: 146:313331
TITLE: Potency of bone marrow mesenchymal stem **cells differentiating** into insulin-positive cells in **vitro** in rats
AUTHOR(S): Wu, Xiaohong; Liu, Cuiping; Mao, Xiaodong; Xu, Kuanfeng; Cui, Dai; Zhu, Jian; Liu, Chao
CORPORATE SOURCE: First Affiliated Hospital, Nanjing Medical University, Nanjing, Jiangsu Province, 210029, Peop. Rep. China
SOURCE: Zhongguo Linchuang Kangfu (**2005**), 9(34), 1-3, 1 plate
CODEN: ZLKHAH; ISSN: 1671-5926
PUBLISHER: Zhongguo Linchuang Kangfu Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The ability of bone marrow mesenchymal stem cells (BM-MSCs) for trans-differentiation into insulin-pos. cells in **vitro** was observed Ten clean-grade male SD rats were selected to sep. and culture the BM-MSCs. The CD45/CD90 expressions and cell cycles were detected by flow cytometry to observe the features of BM-MSCs. The 3-passage cells were gained and divided randomly into 2 groups, low glucose induced group (**DMEM** medium with 5.6 mmol/L glucose) or high glucose induced group (**DMEM** medium with 25 mmol/L glucose), and then cultured for 14 days. The foetus ox serum low glucose was used to change the medium with the volume fraction of 0.05 **DMEM** + nicotinamide (10 mmol/L) for 7 days, adding Exendin-4 (10 nmol/L) induced for 7 days. The expressions of pancreatic and duodenal homeobox 1 (PDX-1), proinsulin and insulin genes were detected with reverse **transcription**-polymerase chain reaction (RT-PCR). The expression of insulin protein was observed with laser confocal microscopy. The number of insulin pos. cells and average fluorescent intensity were detected with flow cytometry. The ultrastructure of cells after inducing was observed with the electromicroscope. BM-MSCs grew adherently to the wall, showing long fusiform. The detection of flow

cytometry showed the CD90 pos. rate was 96.3%, and the CD45 pos. rate was 0.3%; it accounted for 76.8% in G0-G1 phase, 11.3% in G2 phase-M phase, and 11.9% in synthesis phase, resp. The cells distributed in mass-cluster shape in the process of BM-MSCs, and small amount of cells collected as a mass with the diameter of 80-200 μm, semi-suspending in the culture bottle. The effective multiple secretory granules in this kind of cell plasm were observed with electromicroscope. There were PDX-1, proinsulin and insulin gene in the low glucose induced group and high glucose induced group. The detection of flow cytometry indicated that the number of insulin pos. cells and average fluorescent intensity in the low glucose induced group and the high glucose induced group were both significantly higher than those before **induction** of BM-MSCs (21.9% and 19.8% vs. 1.4%; 21.0 and 22.5 vs. 8.7). Thus, the BM-MSCs in rats may be differentiated into insulin-pos. cells in **vitro**.

L31 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1156612 HCAPLUS Full-text
DOCUMENT NUMBER: 142:71213
TITLE: Generation of mammalian β-cells from exocrine pancreas in the presence of **EGF** and LIF for the treatment of diabetes by islet transplantation
INVENTOR(S): Bouwens, Luc; Baeyens, Luc
PATENT ASSIGNEE(S): Vrije Universiteit Brussel, Belg.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004113512	A2	20041229	WO 2004-BE89	20040621 <--
WO 2004113512	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2527626	A1	20041229	CA 2004-2527626	20040621 <--
EP 1636348	A2	20060322	EP 2004-737673	20040621 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2007520194	T	20070726	JP 2006-515565	20040621 <--
PRIORITY APPLN. INFO.:			EP 2003-447164 A	20030620 <--
			WO 2004-BE89 W	20040621 <--

AB The present invention discloses an in **vitro** method wherein mammalian beta-**cell differentiation** can be induced in dedifferentiated exocrine pancreatic cells in a medium comprising ligands of the **EGF** receptor and the GP130 receptor, such as **EGF** and LIF. Insulin secreting cells, obtainable by this method, provide a means for the treatment of diabetes by islet transplantation.

L31 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:1059601 HCAPLUS Full-text
DOCUMENT NUMBER: 142:729
TITLE: In **vitro** platform for screening agents inducing **islet cell** neogenesis
INVENTOR(S): Rosenberg, Lawrence
PATENT ASSIGNEE(S): McGill University, Can.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004106921	A2	20041209	WO 2004-CA788	20040527 <--
WO 2004106921	A3	20050609		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2567823	A1	20041209	CA 2004-2567823	20040527 <--
EP 1631822	A2	20060308	EP 2004-734986	20040527 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007009882	A1	20070111	US 2005-558191	20051125 <--
PRIORITY APPLN. INFO.:			US 2003-473153P P	20030527 <--
			WO 2004-CA788 W	20040527 <--

AB The invention discloses an in **vitro** method for screening agents inducing **islet cell** neogenesis or **duct**-to- **islet cell transdifferentiation**, which comprises (a) expanding in **vitro** cells of a **duct**-like structure obtained by inducing cystic formation in cells in or associated with post-natal islets of Langerhans; (b) treating the expanded cells of said **duct**-like structure with an agent screened; and (c) determining potency of the agent of inducing **islet cell differentiation** of the **duct**-like structure in becoming insulin-producing cells.

L31 ANSWER 17 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2004:327424 USPATFULL Full-text
TITLE: Methods, compositions, and growth and differentiation factors for insulin-producing cells
INVENTOR(S): Scharp, David William, Mission Viejo, CA, UNITED STATES
Latta, Paul Presley, Irvine, CA, UNITED STATES
Coutts, Margaret, Irvine, CA, UNITED STATES
McIntyre, Catherine Anne, Aliso Viejo, CA, UNITED STATES
Presnell, Sharon C., Raleigh, NC, UNITED STATES
Heidaran, Mohammad A., Cary, NC, UNITED STATES
Haaland, Perry D., Chapel Hill, NC, UNITED STATES

NUMBER	KIND	DATE

PATENT INFORMATION: US 2004259244 A1 20041223 <--
APPLICATION INFO.: US 2004-800813 A1 20040315 (10)
RELATED APPLN. INFO.: Continuation of Ser. No. US 2003-447319, filed on 28 May 2003, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-384000P	20020528 (60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KNOBBE MARTENS OLSON & BEAR LLP, 2040 MAIN STREET, FOURTEENTH FLOOR, IRVINE, CA, 92614
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Page(s)
LINE COUNT: 3289
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of converting differentiated non-hormone producing pancreatic cells into differentiated hormone producing cells is disclosed. The method comprises two steps: first, culturing cells under conditions which convert differentiated non-hormone producing cells into stem cells; and second, culturing stem cells under conditions which provide for differentiating stem cells into hormone-producing cells. The invention defines growth and differentiation factors that are presented to the stem cells to result in their differentiation into hormone-producing cells, especially insulin-producing cells. The invention provides a new source of large quantities of hormone producing cells such as insulin-producing cells that are riot currently available for therapeutic uses such as the treatment of diabetes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L31 ANSWER 18 OF 28 USPATFULL on STN
ACCESSION NUMBER: 2004:291766 USPATFULL Full-text
TITLE: Methods and reagents for treating glucose metabolic disorders
INVENTOR(S): Pang, Kevin, Belmont, MA, UNITED STATES
Lu, Kuanghui, Brookline, MA, UNITED STATES
PATENT ASSIGNEE(S): Curis, Inc., Cambridge, MA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004228846	A1	20041118 <--
APPLICATION INFO.:	US 2004-855676	A1	20040527 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-634363, filed on 9 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-499526, filed on 10 Feb 2000, PENDING Continuation-in-part of Ser. No. US 2000-500817, filed on 10 Feb 2000, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-119577P	19990210 (60) <--
	US 1999-119575P	19990210 (60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ROPES & GRAY LLP, ONE INTERNATIONAL PLACE, BOSTON, MA, 02110-2624
NUMBER OF CLAIMS: 50
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 16 Drawing Page(s)
LINE COUNT: 3062
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to methods for potentiating, enhancing or restoring glucose responsivity in pancreatic islets or cells. The methods can be used as therapies for diseases caused by, or coincident with, aberrant glucose metabolism, such as Type II Diabetes Mellitus.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L31 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1152704 HCAPLUS Full-text
DOCUMENT NUMBER: 142:476408
TITLE: Transdifferentiation molecular pathways of neonatal pig pancreatic **duct** cells into endocrine cell phenotypes
AUTHOR(S): Basta, G.; Racanicchi, L.; Mancuso, F.; Guido, L.; Luca, G.; Macchiarulo, G.; Brunetti, P.; Calafiore, R.
CORPORATE SOURCE: Department of Internal Medicine, Section of Internal Medicine and Endocrine and Metabolic Sciences, University of Perugia, Perugia, Italy
SOURCE: Transplantation Proceedings (**2004**), 36(9), 2857-2863
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Restrictions in availability of cadaveric **human** donor pancreata have intensified the search for alternate sources of pancreatic endocrine tissue. The authors have undertaken to assess whether nonendocrine pancreatic tissue, with special regard to **ducts**, including epithelial cells, and retrieved from neonatal pig pancreata that are used for islet isolation, may under special in **vitro** culture conditions generate endocrine cell phenotypes. Special care was taken to identify the time-related appearance of mol. and biochem. markers associated with β-cell specificity, in terms of glucose-sensing apparatus and insulin secretion. For this purpose, established **ductal** origin monolayer cell cultures were incubated with a battery of mono- or polyvalent **growth factors**. Morphol., immunocytochem., mol., and functional assays indicated that under special culture conditions **ductal** origin cells acquired an endocrine identity, based upon expression of key gene **transcripts** that govern the stimulus-coupled insulin secretory activity. Among factors eliciting transdifferentiation of **ductal** epithelial into endocrine cells, Sertoli cell (SC)-conditioned medium seemed to be the most powerful inducer of this process. In fact, the resulting cultures not only expressed β-cell-oriented metabolic markers but also were associated with insulin and C-peptide output at equimolar ratios. This finding indicates that SC coincubation, more than other conditions, caused originally **ductal** cell cultures to gradually differentiate and mature into β-cell-like elements. In vivo studies with this early **cell differentiation product** will test whether our approach may be suitable for correction of hyperglycemia in diabetic animal models.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:343691 HCAPLUS Full-text
DOCUMENT NUMBER: 141:82655
TITLE: Neonatal pig pancreatic **duct**-derived insulin-producing cells: preliminary in **vitro**

studies
AUTHOR(S): Basta, G.; Racanicchi, L.; Mancuso, F.; Guido, L.; Macchiarulo, G.; Luca, G.; Calabrese, G.; Brunetti, P.; Calafiore, R.
CORPORATE SOURCE: Department of Internal Medicine, Section of Internal Medicine and Endocrine and Metabolic Sciences, University of Perugia, Perugia, Italy
SOURCE: Transplantation Proceedings (**2004**), 36(3), 609-611
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neonatal pig pancreata could represent an ideal tissue resource for donor islets for transplantation trials. Because functional islet β-cells could derive from precursors situated in the **ductal** system, and neonatal animals are better suitable than adults for recovering such elements, the authors have examined whether isolated neonatal pancreatic **ducts** (NPD) could form insulin-producing cells. NPD, retrieved from the pancreas by collagenase digestion, were cultured for 2 wk. A compact tissue monolayer detached by trypsin was re-incubated to form upon culture. The primary tissue monolayer was plated, yielding secondary monolayers that were supplemented in culture with the following factors: insulin transferrin selenium, niacinamide, keratinocyte **growth factor**, and high glucose, which promoted formation of **islet cell**-like clusters during 30 days of culture. Upon reaching 50 to 100 μm in diameter, the cell clusters were subjected to morphol. examination (assessment of viability by staining with ethidium bromide+fluorescein diacetate [EB+FD]; staining for insulin with diphenylthiocarbazone [DTZ]); DNA assay; insulin RIA both in the basal state and after in **vitro** static incubation with high glucose; immunolabeling with anti-insulin fluorescent antibodies. Of the cell clusters, 80% were composed of viable cells that faintly showed DTZ staining. Basal insulin was 16.7 μU/mL, but no insulin response was elicited by stimulation with high glucose. Acid-ethanol extraction showed high insulin levels in the clusters. Finally, immunofluorescence for insulin was pos., indicating the presence of β-cell-like committed elements. In conclusion, NPD may differentiate into insulin-producing cells, which are at a very early stage when the glucose-sensing apparatus is still immature.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:459257 HCAPLUS Full-text
DOCUMENT NUMBER: 144:84726
TITLE: Expression of progenitor cell markers during expansion of sorted **human** pancreatic beta cells
AUTHOR(S): Bouckenooghe, Thomas; Vandewalle, Brigitte; Moerman, Ericka; Danze, Pierre-Marie; Lukowiak, Bruno; Muharram, Ghaffar; Kerr-Conte, Julie; Gmyr, Valery; Laine, Bernard; Pattou, Francois
CORPORATE SOURCE: Faculty of Medicine, INSERM ERIT-M 0106, Lille, 59045, Fr.
SOURCE: Gene Expression (**2004**), 12(2), 83-98
CODEN: GEEXEJ; ISSN: 1052-2166
PUBLISHER: Cognizant Communication Corp.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Functional pancreatic beta cell mass is dynamic and although fully differentiated, beta cells are capable of reentering the cell cycle upon appropriate stimuli. Stimulating regeneration-competent cells in situ is

clearly the most desirable way to restore damaged tissue. Regeneration by dedifferentiation and transdifferentiation is a potential source of cells exhibiting a more developmentally immature phenotype and a wide differentiation potential. In this context and to gain a better understanding of the transformation induced in **human** beta cells during forced in **vitro** expansion, we focused on identifying differences in gene expression along with phenotypical transformation between proliferating and quiescent **human** beta cells. FACS-purified beta cells from three different **human** pancreata were cultured during 3-4 mo (8-10 subcultures) on HTB-9 cell matrix with hepatocyte **growth factor**. Gene expression profiling was performed on cells from each subculture on "inhouse" pancreas-specific microarrays consisting of 218 genes and concomitant morphol. transformations were studied by immunocytochem. Immunocytochem. studies indicated a shift from epithelial to neuroepithelial cell phenotype, including progenitor cell features such as protein gene **product** 9.5 (PGP 9.5), Reg, vimentin, and neurogenin 3 protein expression. The expression of 49 genes was downregulated, including several markers of endocrine differentiation while 76 were induced by cell expansion including several markers of progenitor cells. Their pattern also argues for the transdifferentiation of beta cells into progenitor cells, demonstrating neuroepithelial features and overexpressing both PBX1, a homeodomain protein that can bind as a heterodimer with PDX1 and could switch the nature of its **transcriptional** activity, and neurogenin 3, a key factor for the generation of endocrine **islet cells**. Our study of the machinery that regulates **human** beta cell expansion and dedifferentiation may help elucidate some of the critical genes that control the formation of adult pancreatic progenitor cells and hence design targets to modify their expression in view of the production of insulin-secreting cells.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 22 OF 28 USPATFULL on STN

ACCESSION NUMBER: 2002:273335 USPATFULL Full-text

TITLE: Agouti polynucleotide compositions and methods of use

INVENTOR(S): Woychik, Richard P., Orinda, CA, UNITED STATES
Bultman, Scott J., Lakewood, OH, UNITED STATES
Michaud, Edward J., UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002151463	A1	20021017	<--
	US 6514747	B2	20030204	
APPLICATION INFO.:	US 2001-781811	A1	20010212 (9)	

RELATED APPLN. INFO.: Division of Ser. No. US 1998-34088, filed on 3 Mar 1998, GRANTED, Pat. No. US 6310034 Continuation-in-part of Ser. No. US 1993-64385, filed on 21 May 1993, ABANDONED

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: GREGORY A. NELSON, AKERMAN, SENTERFITT AND EIDSON, P.A., 222 LAKEVIEW AVENUE, SUITE 400, P.O.BOX 3188, WEST PALM BEACH, FL, 33402-3188

NUMBER OF CLAIMS: 50

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 41 Drawing Page(s)

LINE COUNT: 11146

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are methods and compositions comprising novel agouti polypeptides and the polynucleotides which encode them. Also disclosed are DNA segments encoding these proteins derived from **human** and murine cell lines, and the use of these polynucleotides and polypeptides in a variety of diagnostic and

therapeutic applications. Methods, compositions, kits, and devices are also provided for identifying compounds which are inhibitors of agouti activity, and for altering fatty acid synthetase activity and intracellular calcium levels in transformed cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L31 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:618143 HCAPLUS Full-text
DOCUMENT NUMBER: 135:192517
TITLE: Pancreatic **islet cell growth factors**
INVENTOR(S): Harrison, Leonard C.; Jiang, Fang-Xu; Stanley, Edouard G.; Gonez, Leonel Jorge
PATENT ASSIGNEE(S): The Walter and Eliza Hall Institute of Medical Research, Australia
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060979	A1	20010823	WO 2001-AU161	20010216 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2400355	A1	20010823	CA 2001-2400355	20010216 <--
US 2002072115	A1	20020613	US 2001-784911	20010216 <--
US 6967100	B2	20051122		
EP 1265985	A1	20021218	EP 2001-905503	20010216 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003523199	T	20030805	JP 2001-560351	20010216 <--
PRIORITY APPLN. INFO.:			US 2000-183573P P	20000218 <--
			WO 2001-AU161 W	20010216 <--

AB The present invention relates generally to **growth factors** and more particularly to **growth factors** which are capable of stimulating or otherwise facilitating formation of insulin-secreting cells. The identification of these **growth factors** permits the development of protocols to culture cells in **vitro** for transplantation into mammalian and in particular **human** subjects with insulin-dependent type 1 diabetes or related conditions. It is further contemplated that the endogenous expression of **growth factors** required for the development of insulin-producing cells may be manipulated in vivo, by the appropriate administration of agents including genetic agents capable of regulating the expression of **growth factors** in pancreatic **duct** epithelial cells. The **growth factors** may also be administered to subjects with type 1 diabetes to stimulate the proliferation and differentiation of pancreatic cells into insulin-secreting cells. The present invention also provides modulators of **growth factor**-mediated pancreatic **cell differentiation**. Such

modulators are useful in the treatment inter alia of β cell tumors and/or pancreatic cancer.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 24 OF 28 USPATFULL on STN

ACCESSION NUMBER:	2001:191105 USPATFULL Full-text
TITLE:	Agouti polypeptide compositions
INVENTOR(S):	Woychik, Richard P., Orinda, CA, United States Bultman, Scott J., Lakewood, OH, United States Michaud, Edward J., Kingston, TN, United States
PATENT ASSIGNEE(S):	UT-Battelle, LLC, Oak Ridge, TN, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6310034	B1	20011030	<--
APPLICATION INFO.:	US 1998-34088		19980303 (9)	

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-64385, filed on 21 May 1993, now abandoned

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Kammerer, Elyabik C.
LEGAL REPRESENTATIVE:	Williams, Morgan & Amerson
NUMBER OF CLAIMS:	34
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	83 Drawing Figure(s); 41 Drawing Page(s)
LINE COUNT:	10935

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are methods and compositions comprising novel agouti polypeptides and the polynucleotides which encode them. Also disclosed are DNA segments encoding these proteins derived from **human** and murine cell lines, and the use of these polynucleotides and polypeptides in a variety of diagnostic and therapeutic applications. Methods, compositions, kits, and devices are also provided for identifying compounds which are inhibitors of agouti activity, and for altering fatty acid synthetase activity and intracellular calcium levels in transformed cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L31 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2001:777489 HCAPLUS Full-text
DOCUMENT NUMBER:	136:51596
TITLE:	**Induction** of pancreatic differentiation by signals from blood vessels
AUTHOR(S):	Lammert, Eckhard; Cleaver, Ondine; Melton, Douglas
CORPORATE SOURCE:	Department of Molecular and Cellular Biology, Howard Highes Medical Institute, Harvard University, Cambridge, MA, 02138, USA
SOURCE:	Science (Washington, DC, United States) (**2001**), 294(5542), 564-567 CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER:	American Association for the Advancement of Science
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Blood vessels supply developing organs with metabolic sustenance. Here, the authors demonstrate a role for blood vessels as a source of developmental signals during pancreatic organogenesis. In **vitro** expts. with embryonic mouse tissues demonstrate that blood vessel endothelium induces insulin expression

in isolated endoderm. Removal of the dorsal aorta in Xenopus laevis embryos results in the failure of insulin expression in vivo. Furthermore, using transgenic mice, the authors show that ectopic vascularization in the posterior foregut leads to ectopic insulin expression and islet hyperplasia. These results indicate that vessels not only provide metabolic sustenance, but also provide **inductive** signals for organ development.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:435042 HCAPLUS Full-text
DOCUMENT NUMBER: 133:308116
TITLE: Modulation of rat pancreatic **acinoductal** transdifferentiation and expression of PDX-1 in **vitro**
AUTHOR(S): Rooman, I.; Heremans, Y.; Heimberg, H.; Bouwens, L.
CORPORATE SOURCE: Department of Experimental Pathology, Free University of Brussels (VUB), Brussels, Belg.
SOURCE: Diabetologia (**2000**), 43(7), 907-914
CODEN: DBTGAJ; ISSN: 0012-186X
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In adult pancreatic regeneration models exocrine acini are found to transdifferentiate to **duct**-like complexes. This has also been associated with the formation of new endocrine **islet cells** . We aimed to establish an in **vitro** model in which this transdifferentiation process is characterized and can be modulated. Purified rat pancreatic acini were cultured in suspension. Differentiation was analyzed by immunocytochem., electron microscopy, western blotting and RT-PCR. During culture acinar cells directly transdifferentiated without dividing, the cells lost their acinar phenotype and started to express cytokeratins 20 and 7 and fetal liver kinase-1 (Flk-1) receptors for vascular endothelial **growth factor**. Expression of the acinar pancreatic exocrine **transcription** factor (PTF-1) remained and the pancreatic duodenal homeobox-containing **transcription** factor (PDX-1) was induced. When transdifferentiation was completed, the cells started to express protein gene **product** 9.5, a pan-neuroendocrine marker. By combining these features, the transdifferentiated cells show similar characteristics to precursor cells during active beta-cell neogenesis. We were able to modulate the differentiation state by addition of nicotinamide or sodium butyrate, agents which are known to stimulate endocrine differentiation in other models. Here, we present an in **vitro** system in which the **cellular differentiation** of putative pancreatic endocrine precursor cells and their PDX-1 expression can be modulated, thereby providing a possible model for the study of beta-**cell transdifferentiation**.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:178307 HCAPLUS Full-text
DOCUMENT NUMBER: 132:292123
TITLE: Reversal of insulin-dependent diabetes using islets generated in **vitro** from pancreatic stem cells
AUTHOR(S): Ramiya, Vijayakumar K.; Maraist, Michael; Arfors, Karl E.; Schatz, Desmond A.; Peck, Ammon B.; Cornelius, Janet G.
CORPORATE SOURCE: Ixion Biotechnology, Alachua, FL, 32615, USA
SOURCE: Nature Medicine (New York) (**2000**), 6(3), 278-282

CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Ductal** structures of the adult pancreas contain stem cells that differentiate into islets of Langerhans. Here, the authors grew pancreatic **ductal** epithelial cells isolated from prediabetic adult non-obese diabetic mice in long-term cultures, where they were induced to produce functioning islets containing α, β and δ cells. These in **vitro**-generated islets showed temporal changes in mRNA **transcripts** for **islet cell**-associated differentiation markers, responded in **vitro** to glucose challenge, and reversed insulin-dependent diabetes after being implanted into diabetic non-obese diabetic mice. The ability to control growth and differentiation of islet stem cells provides an abundant islet source for β-cell reconstitution in type I diabetes.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:30686 HCAPLUS Full-text
DOCUMENT NUMBER: 130:205230
TITLE: Beta cell proliferation and **growth factors**
AUTHOR(S): Nielsen, Jens Hoiriis; Svensson, Carina; Galsgaard, Elisabeth Douglas; Moldrup, Annette; Billestrup, Nils
CORPORATE SOURCE: Hagedorn Research Institute, Gentofte, DK-2820, Den.
SOURCE: Journal of Molecular Medicine (Berlin) (**1999**), 77(1), 62-66
CODEN: JMLME8; ISSN: 0946-2716
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 49 refs. Formation of new beta cells can take place by two pathways: replication of already differentiated beta cells or neogenesis from putative islet stem cells. Under physiol. conditions both processes are most pronounced during the fetal and neonatal development of the pancreas. In adulthood little increase in the beta cell number seems to occur. In pregnancy, however, a marked hyperplasia of the beta cells is observed both in rodents and man. Increased mitotic activity has been seen both in vivo and in **vitro** in islets exposed to placental lactogen (PL), prolactin (PRL) and growth hormone (GH). Receptors for both GH and PRL are expressed in **islet cells** and are upregulated during pregnancy. By mutational anal. the authors have identified different functional domains of the cytoplasmic part of the GH receptor. Thus the mitotic signaling only requires the membrane proximal part of the receptor and activation of the tyrosine kinase JAK2 and the **transcription** factors STAT1 and 3. The activation of the insulin gene however also requires the distal part of the receptor and activation of calcium uptake and STAT5. To identify putative autocrine **growth factors** or targets for **growth factors** the authors have cloned a novel GH/PRL stimulated rat **islet** gene **product**, Pref-1 (preadipocyte factor-1). This protein contains six **EGF**-like motifs and may play a role both in embryonic pancreas differentiation and in beta cell growth and function. In summary, the increasing knowledge about the mechanisms involved in beta **cell differentiation** and proliferation may lead to new ways of forming beta cells for treatment of diabetes in man.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RESULTS FROM MEDLINE, BIOSIS, EMBASE, JAPIO, AND WPIDS

```
=> d que stat l33
L5             1 SEA FILE=REGISTRY ABB=ON  "DMEM/F.12"/CN
L6         25766 SEA FILE=HCAPLUS ABB=ON  ?PANCREATIC?(W)?ISLET?(3W)?LANGERHANS?
                  OR ?ISLET?(W)?CELL?
L7          2869 SEA FILE=HCAPLUS ABB=ON  L6 AND ?TRANSCRIPT?
L8           403 SEA FILE=HCAPLUS ABB=ON  L7 AND ?VITRO?
L9           127 SEA FILE=HCAPLUS ABB=ON  L8 AND ?CELL?(W)?DIFFER?
L10           67 SEA FILE=HCAPLUS ABB=ON  L9 AND ?DUCT?
L11           14 SEA FILE=HCAPLUS ABB=ON  L9 AND ?DUCT?(4A)?ISLET?
L13           67 SEA FILE=HCAPLUS ABB=ON  L10 OR L11
L15           23 SEA FILE=HCAPLUS ABB=ON  L13 AND ?GROWTH?(W)?FACTOR?
L18            4 SEA FILE=HCAPLUS ABB=ON  L13 AND (L5 OR DMEM)
L19            4 SEA FILE=HCAPLUS ABB=ON  L13 AND (L5 OR DMEM?)
L20           24 SEA FILE=HCAPLUS ABB=ON  L15 OR L18 OR L19
L21            7 SEA FILE=HCAPLUS ABB=ON  L20 AND (EGF OR ?CHOLERA?(W)?TOXIN?)
L22           24 SEA FILE=HCAPLUS ABB=ON  L20 OR L21
L23           15 SEA FILE=HCAPLUS ABB=ON  L22 AND ?HUMAN?
L24           24 SEA FILE=HCAPLUS ABB=ON  L22 OR L23
L25           21 SEA FILE=HCAPLUS ABB=ON  L24 AND (PRD<20051125 OR PD<20051125)
L32           19 SEA L25
L33           13 DUP REMOV L32 (6 DUPLICATES REMOVED)


=> d ibib abs l33 1-13

L33  ANSWER 1 OF 13  WPIDS COPYRIGHT 2007       THE THOMSON CORP on STN
ACCESSION NUMBER:     2005-225138 [24]   WPIDS
DOC. NO. CPI:         C2005-072246 [24]
DOC. NO. NON-CPI:     N2005-185412 [24]
TITLE:                Preparing embryonic stem cells for treating, e.g.
                      insulin-dependent diabetes, Parkinson's disease,
                      Huntington's disease, by culturing the cells obtained
                      from the inner cell mass of a blastocyst to obtain
                      embryonic stem cells
DERWENT CLASS:        B04; D16; P14
INVENTOR:             ESPLUGUES MOTA J V; PELLICER MARTIN A; SIMON VALLES C
PATENT ASSIGNEE:      (CNIC-N) CNIC FUNDACION CENT NACIONAL INVESTIGACI;
                      (IVIP-N) FUNDACION IVI PARA EL ESTUDIO REPRODUCCI
COUNTRY COUNT:        31

PATENT INFO ABBR.:

      PATENT NO      KIND DATE     WEEK     LA  PG          MAIN IPC
      ------------------------------------------------------------------
      EP 1516925      A1 20050323 (200524)* EN  25[1]                    <--

APPLICATION DETAILS:

      PATENT NO      KIND                  APPLICATION    DATE
      ------------------------------------------------------------------
      EP 1516925 A1                        EP 2003-380205 20030918

PRIORITY APPLN. INFO: EP 2003-380205 20030918
AN   2005-225138 [24]   WPIDS
AB    EP 1516925 A1   UPAB: 20060122
```

NOVELTY - Preparing embryonic stem cells comprises: (a) providing a tripronucleated zygote; (b) removing one of the pronuclei to provide a diploid heteroparental zygote;
(c) culturing the diploid zygote to produce a blastocyst; (d) obtaining one or more cells from the inner cell mass of the blastocyst; and
(e) culturing the cells obtained from the inner cell mass to obtain embryonic stem cells.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) preparing a desired cell; (2) an embryonic stem (ES) cell derived from a tripronucleated zygote;
(3) a differentiated cell obtained by the method above; (4) a method of therapy;
(5) a pharmaceutical composition comprising a cell above; (6) preparing a secreted factor of interest; (7) preparing nucleic acid from a cell; (8) preparing a panel of cells; (9) a panel of cells obtained by the process above; (10) testing the effect(s) of a test material on a cell of interest; (11) an in **vitro** screening assay; and (12) preparing a genetically-modified ES cell. ACTIVITY - Antidiabetic; Antiparkinsonian; Anticonvulsant; Nootropic; Neuroprotective; Cardiant; Hepatotropic; Osteopathic; Antiarthritic.
No biological data given.
MECHANISM OF ACTION - None given.
USE - The ES cell is useful for transdifferentiation of a **human** cell in **vitro** or in vivo. The cell is also useful in medicine, or in the manufacture of a medicament. The panel is useful for assessing toxic effects, metabolism, allergic reactions, side effects, biodistribution, inflammatory reactions, contact reactions, or dermatological effects or a material. (All claimed.) The method is useful for preparing embryonic stem cells from triploid zygotes. Stem cell and their **products** can be used to treat diseases, including insulin-dependent diabetes, Parkinson's disease, Huntington's disease, spinal cord injury, amyotrophic lateral sclerosis, Alzheimer's disease, myocardial infarction, ischemic cardiac tissue or heart failure; side effects of radiation; corneal scarring; liver cirrhosis or failure; ischemic brain damage; spinal cord damage; cartilage damage; bone damage; osteoarthritis; myelination disorders, such as Pelizaeus-Merzbacher disease, multiple sclerosis, adenoleukodystrophies, neuritis and neuropathies.

L33 ANSWER 2 OF 13 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER:	2005246958 EMBASE Full-text
TITLE:	Molecular targeting of pancreatic disorders.
AUTHOR:	Tamada K.; Wang X.-P.; Brunicardi F.C.
CORPORATE SOURCE:	Dr. F.C. Brunicardi, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, United States
SOURCE:	World Journal of Surgery, (**2005**) Vol. 29, No. 3, pp. 325-333. . Refs: 119 ISSN: 0364-2313 CODEN: WJSUDI
COUNTRY:	United States
DOCUMENT TYPE:	Journal; Conference Article
FILE SEGMENT:	022 Human Genetics 037 Drug Literature Index 038 Adverse Reactions Titles 039 Pharmacy 048 Gastroenterology
LANGUAGE:	English
SUMMARY LANGUAGE:	English
ENTRY DATE:	Entered STN: 30 Jun 2005 Last Updated on STN: 30 Jun 2005

AB During the last decade significant advances in gene therapy have made it possible to treat various pancreatic disorders in both animal models and in **humans**. For example, insulin gene delivery to non-β-cell tissues has been shown to reverse hyperglycemia in diabetic mice, and islet transplantation, based on in **vitro** differentiation of β cells and concomitant gene targeting to prevent host autoimmune responses, has become more feasible. Additionally, **introduction** of the glucokinase regulatory protein and protein kinase C-ζ have been shown to improve glucose tolerance in non-insulin-dependent diabetes mellitus animal models. Pancreatic cancer studies utilize several DNA-based strategies for tumor treatment including **introduction** of tumor suppressor genes, suppression of oncogenes, suicide gene/prodrug therapy, and restricted replication-competent virus therapy. Tumor-specific targeting is an important part of suicide gene therapy, and tumor-specific promoters are used for cell-specific targeting. Tumor-specific suicide gene therapy directed by the rat insulin promoter has been used to eliminate insulinoma tumors in a mouse model. This review compiles a compendium of information related to the treatment of pancreatic disorders using gene therapy. .COPYRGT. 2005 by the Socie te Internationale de Chirurgie.

L33 ANSWER 3 OF 13 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005471900 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16138828
TITLE: Metaplasia in the pancreas.
AUTHOR: Lardon Jessy; Bouwens Luc
CORPORATE SOURCE: Cell Differentiation Unit, Diabetes Research Center, Free University of Brussels, Vrije Universiteit Brussel, Laarbeeklaan 103, B-1090 Brussels, Belgium.
SOURCE: Differentiation; research in biological diversity, **(2005 Jul)** Vol. 73, No. 6, pp. 278-86. Ref: 111
Journal code: 0401650. ISSN: 0301-4681.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200511
ENTRY DATE: Entered STN: 7 Sep 2005
Last Updated on STN: 15 Nov 2005
Entered Medline: 14 Nov 2005

AB There is currently much interest in the possibility to treat chronic diseases by cell replacement or regenerative therapies. Most of these studies focus on the manipulation of undifferentiated stem cells. However, tissue repair and regeneration can also be achieved by differentiated cells, which, in certain conditions, can even transdifferentiate to other cell types. Such transdifferentiations can lead to tissue metaplasia. The pancreas is an organ wherein metaplasia has been well investigated and for which experimental models have been recently developed allowing to unravel the molecular basis of transdifferentiation. Pancreatic metaplasias studied so far include the conversion of exocrine acinar cells to **duct** cells, exocrine cells to endocrine **islet cells**, endocrine cells to **duct** cells, and acinar cells to hepatocytes. Epitheliomesenchymal transitions have also been described. The available evidence indicates that mature cells can be reprogrammed by specific environmental cues inducing the expression of cell type-specific **transcription** factors. For example, the glucocorticoid hormone dexamethasone induces pancreatic transdifferentiation to hepatocytes, whereas the combination of epidermal **growth factor** and leukemia-inhibitory factor induces exocrine-endocrine transdifferentiation in **vitro**. Further unravelling of the involved signal **transduction** pathways, **transcription** factor networks, and chromatin

modifications is required to manipulate metaplasia at will and to apply it in tissue repair or regeneration.

L33 ANSWER 4 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2005252665 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15892450
TITLE: Expression of progenitor cell markers during expansion of sorted **human** pancreatic beta cells.
AUTHOR: Bouckenooghe Thomas; Vandewalle Brigitte; Moerman Ericka; Danze Pierre-Marie; Lukowiak Bruno; Muharram Ghaffar; Kerr-Conte Julie; Gmyr Valery; Laine Bernard; Pattou Francois
CORPORATE SOURCE: INSERM ERIT-M 0106, Faculty of Medicine, Place de Verdun, 59045 Lille, France.
SOURCE: Gene expression, **(2005)** Vol. 12, No. 2, pp. 83-98.
Journal code: 9200651. ISSN: 1052-2166.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 17 May 2005
Last Updated on STN: 17 Jun 2005
Entered Medline: 16 Jun 2005

AB Functional pancreatic beta cell mass is dynamic and although fully differentiated, beta cells are capable of reentering the cell cycle upon appropriate stimuli. Stimulating regeneration-competent cells in situ is clearly the most desirable way to restore damaged tissue. Regeneration by dedifferentiation and transdifferentiation is a potential source of cells exhibiting a more developmentally immature phenotype and a wide differentiation potential. In this context and to gain a better understanding of the transformation induced in **human** beta cells during forced in **vitro** expansion, we focused on identifying differences in gene expression along with phenotypical transformation between proliferating and quiescent **human** beta cells. FACS-purified beta cells from three different **human** pancreata were cultured during 3-4 months (8-10 subcultures) on HTB-9 cell matrix with hepatocyte **growth factor**. Gene expression profiling was performed on cells from each subculture on "in-house" pancreas-specific microarrays consisting of 218 genes and concomitant morphological transformations were studied by immunocytochemistry. Immunocytochemical studies indicated a shift from epithelial to neuroepithelial cell phenotype, including progenitor cell features such as protein gene **product** 9.5 (PGP 9.5), Reg, vimentin, and neurogenin 3 protein expression. The expression of 49 genes was downregulated, including several markers of endocrine differentiation while 76 were induced by cell expansion including several markers of progenitor cells. Their pattern also argues for the transdifferentiation of beta cells into progenitor cells, demonstrating neuroepithelial features and overexpressing both PBX1, a homeodomain protein that can bind as a heterodimer with PDX1 and could switch the nature of its **transcriptional** activity, and neurogenin 3, a key factor for the generation of endocrine **islet cells**. Our study of the machinery that regulates **human** beta cell expansion and dedifferentiation may help elucidate some of the critical genes that control the formation of adult pancreatic progenitor cells and hence design targets to modify their expression in view of the **production** of insulin-secreting cells.

L33 ANSWER 5 OF 13 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:99334 BIOSIS Full-text
DOCUMENT NUMBER: PREV200500101635
TITLE: Transdifferentiation molecular pathways of neonatal pig pancreatic **duct** cells into endocrine cell phenotypes.
AUTHOR(S): Basta, G.; Racanicchi, L.; Mancuso, F.; Guido, L.; Luca, G.; Macchiarulo, G.; Brunetti, P.; Calafiore, R. [Reprint Author]
CORPORATE SOURCE: DiMIDept Internal MedSect Internal Med and Endocrine and Metab Sci, Univ Perugia, Via E Dal Pozzo, I-06126, Perugia, Italy
islet@unipg.it
SOURCE: Transplantation Proceedings, (**November 2004**) Vol. 36, No. 9, pp. 2857-2863. print.
CODEN: TRPPA8. ISSN: 0041-1345.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Mar 2005
Last Updated on STN: 9 Mar 2005

AB Restrictions in availability of cadaveric **human** donor pancreata have intensified the search for alternate sources of pancreatic endocrine tissue. We have undertaken to assess whether nonendocrine pancreatic tissue, with special regard to **ducts**, including epithelial cells, and retrieved from neonatal pig pancreata that are used for islet isolation, may under special in **vitro** culture conditions generate endocrine cell phenotypes. Special care was taken to identify the time-related appearance of molecular and biochemical markers associated with beta-cell specificity, in terms of glucose-sensing apparatus and insulin secretion. For this purpose, established **ductal** origin monolayer cell cultures were incubated with a battery of mono- or polyvalent **growth factors**. Morphological, immunocytochemical, molecular, and functional assays indicated that under special culture conditions **ductal** origin cells acquired an endocrine identity, based upon expression of key gene **transcripts** that govern the stimulus-coupled insulin secretory activity. Among factors eliciting transdifferentiation of **ductal** epithelial into endocrine cells, Sertoli cell (SC)-conditioned medium seemed to be the most powerful inducer of this process. In fact, the resulting cultures not only expressed beta-cell-oriented metabolic markers but also were associated with insulin and C-peptide output at equimolar ratios. This finding indicates that SC coincubation, more than other conditions, caused originally **ductal** cell cultures to gradually differentiate and mature into beta-cell-like elements. In vivo studies with this early **cell differentiation product** will test whether our approach may be suitable for correction of hyperglycemia in diabetic animal models.

L33 ANSWER 6 OF 13 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005188486 EMBASE Full-text
TITLE: Expression of progenitor cell markers during expansion of sorted **human** pancreatic beta cells.
AUTHOR: Bouckenooghe T.; Vandewalle B.; Moerman E.; Danze P.-M.; Lukowiak B.; Muharram G.; Kerr-Conte J.; Gmyr V.; Laine B.; Pattou F.
CORPORATE SOURCE: B. Vandewalle, INSERM, ERIT-M 0106, Faculte de Medecine, Place de Verdun, 59045 Lille, France. bvandewalle@univ-lille2.fr
SOURCE: Gene Expression, (**2004**) Vol. 12, No. 2, pp. 83-98. .
Refs: 53
ISSN: 1052-2166 CODEN: GEEXEJ

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 May 2005
Last Updated on STN: 19 May 2005

AB Functional pancreatic beta cell mass is dynamic and although fully differentiated, beta cells are capable of reentering the cell cycle upon appropriate stimuli. Stimulating regeneration-competent cells in situ is clearly the most desirable way to restore damaged tissue. Regeneration by dedifferentiation and transdifferentiation is a potential source of cells exhibiting a more developmentally immature phenotype and a wide differentiation potential. In this context and to gain a better understanding of the transformation induced in **human** beta cells during forced in **vitro** expansion, we focused on identifying differences in gene expression along with phenotypical transformation between proliferating and quiescent **human** beta cells. FACS-purified beta cells from three different **human** pancreata were cultured during 3-4 months (8-10 subcultures) on HTB-9 cell matrix with hepatocyte **growth factor**. Gene expression profiling was performed on cells from each subculture on "in-house" pancreas-specific microarrays consisting of 218 genes and concomitant morphological transformations were studied by immunocytochemistry. Immunocytochemical studies indicated a shift from epithelial to neuroepithelial cell phenotype, including progenitor cell features such as protein gene **product** 9.5 (PGP 9.5), Reg, vimentin, and neurogenin 3 protein expression. The expression of 49 genes was downregulated, including several markers of endocrine differentiation while 76 were induced by cell expansion including several markers of progenitor cells. Their pattern also argues for the transdifferentiation of beta cells into progenitor cells, demonstrating neuroepithelial features and overexpressing both PBX1, a homeodomain protein that can bind as a heterodimer with PDX1 and could switch the nature of its **transcriptional** activity, and neurogenin 3, a key factor for the generation of endocrine **islet cells**. Our study of the machinery that regulates **human** beta cell expansion and dedifferentiation may help elucidate some of the critical genes that control the formation of adult pancreatic progenitor cells and hence design targets to modify their expression in view of the **production** of insulin-secreting cells. Copyright .COPYRGT. 2005 Cognizant Comm. Corp.

L33 ANSWER 7 OF 13 WPIDS COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-315106 [35] WPIDS
DOC. NO. CPI: C2002-091601 [35]
TITLE: Use of phosphatidylinositol 3-kinase (PI3K) inhibitors to produce endocrine cells useful for producing hormones (e.g. insulin) for treating e.g. diabetes
DERWENT CLASS: B04; D16
INVENTOR: BEATTIE G M; HAYEK A; PTASZNIK A
PATENT ASSIGNEE: (BEAT-I) BEATTIE G M; (HAYE-I) HAYEK A; (PTAS-I) PTASZNIK A; (REGC-C) UNIV CALIFORNIA
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC	
US 20020037276	A1	20020328	(200235)*	EN	1[0]		<--
							<--
US 6413773	B1	20020702	(200248)	EN			<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20020037276 A1	Provisional	US 1998-87558P	19980601
US 20020037276 A1	Provisional	US 1998-87730P	19980602
US 20020037276 A1		US 1999-320479	19990526

PRIORITY APPLN. INFO: **US 1999-320479 19990526**
US 1998-87558P 19980601
US 1998-87730P 19980602

AN 2002-315106 [35] WPIDS

AB US 20020037276 A1 UPAB: 20050525

NOVELTY - Using phosphatidylinositol 3-kinase (PI3K) inhibitors to produce endocrine cells from precursor cells, is new. The cells may be cultured to produce hormonal **products**, especially insulin, for the treatment of endocrine diseases, especially diabetes.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) a method (I) of inducing differentiation of endocrine cells, comprising culturing a mammalian endocrine precursor cell in the presence of a phosphatidylinositol 3-kinase (PI3K) inhibitor so that the endocrine precursor **cell differentiates** into a cell having endocrine activity;
(2) a nutrient medium (II) for use in the culture of differentiated mammalian cells having endocrine activity, comprising a mammalian cell culture medium and a phosphatidylinositol 3-kinase inhibitor; (3) a process (III) for obtaining animal cells by cell culture, comprising:
(a) culturing mammalian precursor cells in a nutrient medium contained in a culture vessel (the nutrient medium comprises a mammalian cell culture medium and a phosphatidylinositol 3-kinase inhibitor (i.e. (II)));
(b) continuing the culture in the nutrient medium until the precursor **cells differentiate** and have endocrine activity; and
(c) collecting the differentiated cells; (4) a bioreactor (IV) comprising a container containing a nutrient medium (the nutrient medium comprises a mammalian cell culture medium and a phosphatidylinositol 3-kinase inhibitor (i.e. (II))) and a mammalian precursor cell capable of endocrine activity when differentiated; (5) a method (V) of treating a hormone deficiency in an organism, comprising culturing a mammalian precursor cell in the presence of a phosphatidylinositol 3-kinase (PI3K) inhibitor (so that the precursor **cell differentiates** into a cell having endocrine activity) and transplanting the cell having endocrine activity into the organism; and
(6) a kit (VI) for the in **vitro** culture of a differentiated endocrine cell, comprising a container containing a phosphatidylinositol 3-kinase (PI3K) inhibitor, cell culture media, adult mammalian cells, fetal mammalian cells, and instructional materials teaching the use of PI3K inhibitors to enhance the differentiation of endocrine cells in culture.

ACTIVITY - Antidiabetic.

MECHANISM OF ACTION - Endocrine; hormonal. To investigate whether PI3K activation is important for endocrine differentiation of **human** fetal pancreatic cells, ICCs were continuously treated for 5 days with 100 nM wortmannin or 10 mM Ly294002, concentrations that block over 90% of total PI3K activity in intact fetal **islet cells**. It was established that these concentrations of wortmannin and Ly294002 almost completely inhibited the rise in PIP3 formation stimulated by **growth factors** in intact (32P)orthophosphate-labeled **islet cells**. By contrast, these concentrations of inhibitors did not affect significantly the ratio of (32P)PIP2 to (32P)PIP and (32P)PIP to (32P)PI in phospholipid labeling experiments where PIP3 levels were measured, implying that other kinases (P15K and P14K) were not inhibited under these conditions. Wortmannin, a fungal metabolite, functioned as a covalent inhibitor of the catalytic p110 subunits of PI3Ks at nanomolar concentrations,

whereas Ly29400 2, a structurally and mechanistically distinct compound, functioned as a noncovalent, competitive inhibitor of PI3Ks at 100 fold higher concentrations than wortmannin (Okada et al. (1994) J. Biol. Chemical 269:3563-3567; Powis et al. (1994) Cancer Res. 54:2419-2423; Vlahos et al. (1994) J. Biol. Chemical 269:5241-5248; Wymann et al. (1996) Mol. Cell. Biol. 16:1722-1733).

At nanomolar concentrations, wortmannin was thought to be selective for PI3K. Ly294002, even at micromolar concentrations, is quite specific for PI3K and did not affect PI4K or a number of intracellular Ser/Thr and Tyr kinases (Vlahos et al. (1994) J. Biol. Chemical 269:5241-5248). It was also shown that continuous treatment for 5 days with 100 nM wortmannin or 10 mM Ly294002 did not cause notable cytotoxity nor induce apoptosis in fetal pancreatic cells growing as islet-like cell clusters. The **transcriptional** expression of islet-specific hormone genes in ICCs g rowing for 5 days in the presence of PI3K inhibitors was measured. Wortmannin and Ly294002 increased the **transcriptional** levels of insulin, glucagon, and somatostatin in cells within the ICCs. The pattern of alterations of mRNA levels was strikingly similar to that of insulin protein. Therefore, these results indicated that two structurally distinct compounds have similar effects on hormone **transcription** as a consequence of their shared ability to function as specific inhibitors of PI3K.

USE - The phosphatidylinositol 3-kinase inhibitors are used to stimulate the differentiation of precursor cells (especially **human** fetal pancreatic cells) into endocrine cells that secrete **products** such as insulin. These cells find a number of uses, for example in the treatment of conditions characterized by a hormone deficiency (e.g. diabetes) comprising a deficiency in insulin and/or glucagon, and/or somatostatin. The method involve culturing a mammalian precursor cell in the presence of a phosphatidylinositol 3-kinase (PI3K) inhibitor so that precursor **cell differentiates** into a cell having endocrine activity, and then transplanting the cell having endocrine activity into the organism. The precursor cell can be virtually any endocrine precursor cell and more preferably is a pancreatic cell (e.g. a beta-cell).

ADVANTAGE - These culture methods provide a way in which large quantities of previously unavailable endocrine positive cells can be obtained.

L33 ANSWER 8 OF 13 WPIDS COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-168791 [17] WPIDS
CROSS REFERENCE: 2002-667000; 2005-458514; 2006-099016; 2007-219481
DOC. NO. CPI: C2001-050465 [17]
TITLE: New multipotent adult stem cells, useful for forming cells of multiple tissue types e.g. for treating cancer and repairing damaged tissue
DERWENT CLASS: B04; D16
INVENTOR: FURCHT L T; MCL LLC; REYES M; VERFAILLIE C M; FURCHT L
PATENT ASSIGNEE: (ATHE-N) ATHERSYS INC; (FURC-I) FURCHT L T; (MCLM-N) MCL LLC; (REYE-I) REYES M; (VERF-I) VERFAILLIE C M; (MINU-C) UNIV MINNESOTA
COUNTRY COUNT: 93

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC	
WO 2001011011	A2	20010215	(200117)*	EN	114[16]		<--
AU 2000066218	A	20010305	(200130)	EN			<--
EP 1226233	A2	20020731	(200257)	EN			<--

```
      JP 2003506075   W  20030218 (200315)  JA  31                    <--
                                                                       <--
      NZ 517002       A  20040625 (200445)  EN                        <--
                                                                       <--
      ZA 2002001125   A  20040728 (200466)  EN  163                   <--
                                                                       <--
      US 20050181502  A1 20050818 (200555)  EN                        <--
      US 20060030041  A1 20060209 (200612)  EN
      US 7015037      B1 20060321 (200621)  EN
      AU 784163       B2 20060216 (200661)  EN
      IN 2002CN00311  P4 20070223 (200729)  EN
```

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001011011	A2	WO 2000-US21387	20000804
US 20050181502	A1 Provisional	US 1999-147324P	19990805
US 20060030041	A1 Provisional	US 1999-147324P	19990805
US 7015037	B1 Provisional	US 1999-147324P	19990805
US 20050181502	A1 Provisional	US 1999-164650P	19991110
US 20060030041	A1 Provisional	US 1999-164650P	19991110
US 7015037	B1 Provisional	US 1999-164650P	19991110
AU 2000066218	A	AU 2000-66218	20000804
AU 784163	B2	AU 2000-66218	20000804
EP 1226233	A2	EP 2000-953840	20000804
NZ 517002	A	NZ 2000-517002	20000804
EP 1226233	A2	WO 2000-US21387	20000804
JP 2003506075	W	WO 2000-US21387	20000804
NZ 517002	A	WO 2000-US21387	20000804
US 20050181502	A1 Cont of	WO 2000-US21387	20000804
US 20060030041	A1 Cont of	WO 2000-US21387	20000804
JP 2003506075	W	JP 2001-515800	20000804
ZA 2002001125	A	ZA 2002-1125	20020208
US 20050181502	A1 Cont of	US 2002-48757	20020821
US 20060030041	A1 Cont of	US 2002-48757	20020821
US 7015037	B1	US 2002-48757	20020821
US 20050181502	A1	US 2005-84256	20050321
US 20060030041	A1	US 2005-238234	20050929
IN 2002CN00311	P4	WO 2000-US21387	20000804
IN 2002CN00311	P4	IN 2002-CN311	20020228

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2000066218	A	Based on	WO 2001011011	A
EP 1226233	A2	Based on	WO 2001011011	A
JP 2003506075	W	Based on	WO 2001011011	A
NZ 517002	A	Based on	WO 2001011011	A
AU 784163	B2	Based on	WO 2001011011	A

PRIORITY APPLN. INFO: **US 1999-164650P 19991110**
US 1999-147324P 19990805
WO 2000-US21387 20000804
US 2002-48757 20020821
US 2005-84256 20050321
US 2005-238234 20050929

AN 2001-168791 [17] WPIDS

CR 2002-667000; 2005-458514; 2006-099016; 2007-219481

AB WO 2001011011 A2 UPAB: 20060116
NOVELTY - An isolated multipotent: (a) mammalian stem cell (I) that is surface antigen negative for CD44, CD45 and **human** leukocyte antigen (HLA) class I and II; (b) non-embryonic, non-germ cell line cell (II) that expresses **transcription** factors oct3/4, REX-1 and ROX-1; and (c) cell (III) derived from a post-natal mammal that responds to **growth factor** leukemia inhibitory factor (LIF) and has LIF receptors, are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a differentiated progeny cell (IV) obtained from (I), (II) or (III), which is a bone, cartilage, adipocyte, fibroblast, marrow stroma, skeletal/smooth/cardiac muscle, endothelial, epithelial, endocrine, exocrine, hematopoietic, glial, neuronal or oligodendrocyte cell; (2) an isolated transgenic multipotent mammalian stem cell (V) comprising (I), (II) or (III), where its genome has been altered by insertion of preselected isolated DNA, by substitution of a cellular genome segment with preselected isolated DNA or by deletion/inactivation of a portion of the cellular genome; (3) a **cell differentiation** solution comprising factors that modulate the level of oct3/4 expression for promoting continued growth or differentiation of undifferentiated multipotent stem cells;
(4) isolating (M1) multipotent adult stem cells (MASC) comprising: (a) depleting bone marrow mononuclear cells of CD45+ glycophorin A+ cells; (b) recovering CD45- glycophorin A- cells; (c) plating the recovered cells onto a matrix coating; and (d) culturing the plated cells in media supplemented with **growth factors**;
(5) culturing (M2) isolated MASC comprising adding the cells to serum free or low serum medium containing insulin, selenium, bovine serum albumin (BSA), linoleic acid, dexamethasone and PDGF; (6) a cultured clonal population of mammalian MASC isolated according to M2;
(7) permanently and/or conditionally immortalizing MASC derived cells and differentiated progeny comprising transferring telomerase into MASC or differentiated progeny; and (8) expanding undifferentiated multipotent stem cells into differentiated hair follicles comprising administering appropriate **growth factors** and growing the cells. ACTIVITY - Ophthalmological; antidiabetic; nootropic; neuroprotective; antiparkinsonian; cardiant; antimicrobial; osteopathic; anti-**human** immuno deficiency virus.
MECHANISM OF ACTION - Gene therapy. No supporting data is given.
USE - Fully allogenic multipotent stem cells, derived hematopoietic stem cells or progenitor cells are useful to induce tolerance in a mammal for subsequence stem cell derived tissue transplants or other organ transplants. (I-III) are useful for: (1) in utero transplantation of (I), (II) or (III) to form chimerism of cells and tissues to produce **human** cells in pre- or post-natal **humans** or animals following transplantation, where (I-III) produce therapeutic enzymes, proteins or other **products** to correct genetic defects;
(2) for gene therapy in a subject in need of therapeutic treatment comprising: (a) genetically altering (I), (II) or (III) by introducing into the cells an isolated pre-selected DNA encoding a desired gene **product** ;
(b) expanding the cells in culture; and (c) introducing the cells into the body of the subject to produce the desired gene **product**;
(3) repairing damaged tissue in a **human** subject comprising:
(a) expanding (I-III) in culture; and (b) contacting expanded (I-III) with the damaged tissue; (4) inducing an immune response to an infectious agent comprising: (a) genetically altering expanded (I), (II) or (III) to express (an) antigenic molecule(s) that elicit a protective immune response against an infectious agent; and
(b) introducing into the subject the genetically altered cells to induce the immune response; and
(5) treating cancer comprising: (a) genetically altering (I), (II) or (III) to express a tumoricidal protein, an anti-angiogenic protein or a protein that is expressed on a tumor cell surface with a protein associated with stimulation

of an immune response to antigen; and (b) introducing the genetically altered (I), (II) or (III) into the mammalian subject.
MASCs are useful for:
(1) identifying genetic polymorphisms associated with physiologic abnormalities comprising:
(a) isolating the MASCs from a statistically significant population of individuals;
(b) culture expanding the MASCs; (c) identifying (a) genetic polymorphism(s) in the cultured MASCs; (d) inducing the cultured MASC to differentiate; and (e) characterizing aberrant metabolic processes associated with the genetic polymorphism(s) by comparing the differentiation pattern exhibited by an MASC with a normal genotype with the differentiation patten exhibited by an MASC with an identified polymorphism; and (2) characterizing celllular responses to biologic or pharmacologic agents comprising:
(a) isolating MASCs from a statistically significant population of individuals;
(b) culture expanding the MASCs; (c) contacting the MASC cultures with (a) biologic or pharmacologic agent(s);
(d) comparing (a) cellular response(s) of the MASC cultures from individuals in the population (all claimed). MASCs are useful for treating various diseases including blindness caused by glaucoma or diabetic retinopathy, degenerative disease (stroke, Parkinson's disease, Alzheimer's disease and Huntington's disease), cardiovascular disease (e.g. heart attacks), metabolic storage disease, infectious disease (e.g. acquired immuno deficiency syndrome), bone diseases (osteoarthritis) and neural diseases.
ADVANTAGE - The MASCs have the ability to differentiate into a wide variety of cell types of different lineages not previously described such as bone, cartilage, adipocyte, fibroblast, marrow stroma, skeletal/cardiac/smooth muscle, endothelial, epithelial, endocrine, exocrine, hematopoietic, glial, neuronal or oligodendrocyte cell.

L33 ANSWER 9 OF 13 WPIDS COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-549143 [50] WPIDS
CROSS REFERENCE: 2002-227148
DOC. NO. CPI: C2000-163961 [50]
TITLE: New pancreatic progenitor cells for regulating the expression of insulin and other beta cell components by differentiating into glucose-responsive, insulin-secreting cells and for treating type 1 diabetes mellitus
DERWENT CLASS: B04; D16
INVENTOR: FUNG B; KAGAN D; LU K; PANG K; RUBIN L
PATENT ASSIGNEE: (CURI-N) CURIS INC; (ESCE-N) ES CELL INT PTE LTD; (ONTO-N) ONTOGENY INC
COUNTRY COUNT: 89

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC	
WO 2000047720	A2	20000817	(200050)*	EN	104[40]		<--
AU 2000036979	A	20000829	(200062)	EN			<--
US 6326201	B1	20011204	(200203)	EN			<--
EP 1175487	A2	20020130	(200216)	EN			<--
JP 2002538779	W	20021119	(200281)	JA	134		<--

AU 780794	B2	20050414	(200530)	EN	<--
					<--
AU 2005203060	A1	20050811	(200557)#	EN	<--
US 20050266555	A1	20051201	(200579)	EN	
IL 144654	A	20061231	(200720)	EN	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000047720	A2	WO 2000-US3419	20000210
US 6326201	B1 Provisional	US 1999-119576P	19990210
US 20050266555	A1 Provisional	US 1999-119576P	19990210
US 6326201	B1 Provisional	US 1999-142305P	19990702
US 20050266555	A1 Provisional	US 1999-142305P	19990702
US 6326201	B1 Provisional	US 1999-171338P	19991221
US 20050266555	A1 Provisional	US 1999-171338P	19991221
AU 2000036979	A	AU 2000-36979	20000210
AU 780794	B2	AU 2000-36979	20000210
EP 1175487	A2	EP 2000-915758	20000210
JP 2002538779	W	JP 2000-598620	20000210
US 6326201	B1	US 2000-499362	20000210
US 20050266555	A1 CIP of	US 2000-499362	20000210
EP 1175487	A2	WO 2000-US3419	20000210
JP 2002538779	W	WO 2000-US3419	20000210
US 20050266555	A1 Cont of	US 2000-635370	20000809
US 20050266555	A1	US 2005-172144	20050630
AU 2005203060	A1	AU 2005-203060	20050714
IL 144654	A	IL 2000-144654	20000210

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 780794	B2	Previous Publ	AU 2000036979	A
AU 2005203060	A1	Div ex	AU 780794	B
US 20050266555	A1	CIP of	US 6326201	B
US 20050266555	A1	Cont of	US 6946293	B
AU 2000036979	A	Based on	WO 2000047720	A
EP 1175487	A2	Based on	WO 2000047720	A
JP 2002538779	W	Based on	WO 2000047720	A
AU 780794	B2	Based on	WO 2000047720	A
IL 144654	A	Based on	WO 2000047720	A

PRIORITY APPLN. INFO: **US 1999-171338P 19991221**
US 1999-119576P 19990210
US 1999-142305P 19990702
US 2000-499362 20000210
US 2000-635370 20000809
US 2005-172144 20050630
AU 2005-203060 20050714

AN 2000-549143 [50] WPIDS
CR 2002-227148
AB WO 2000047720 A2 UPAB: 20060202
NOVELTY - A substantially pure population of viable pancreatic progenitor cells (PPC) characterized by expression of a **transcription** factor that regulates expression of insulin and other beta cell components (PDX1) and able to differentiate into glucose-responsive, insulin-secreting cells, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a cellular composition comprising, as the cellular component, a substantially pure population of viable PCC capable of proliferation and/or differentiation in a culture medium; (2) a cellular composition comprising 75 percent progenitor cells being isolated from pancreatic **ductal** epithelium or the progeny of them, which are capable of self-regeneration in a culture medium; (3) a cellular composition comprising viable PCC capable of self-regeneration in a culture medium and differentiation to members of the pancreatic lineages;
(4) a cellular composition comprising PPC capable of self-regeneration in a culture medium and differentiation to members of the pancreatic lineages, with fewer than 20 percent of lineage committed cells;
(5) isolating (A) progenitor cells comprising: (i) obtaining pancreatic **ductal** cells; (ii) culturing the pancreatic cells in nutrient medium; and (iii) isolating a population of progenitor cells from the culture; (6) a cellular composition as in (2), where the cells are isolated (B) by:
(a) obtaining dissociated epithelial cells from pancreatic **ducts**;
(b) culturing, as a monolayer, the epithelial cells in nutrient medium to expand pancreatic progenitors from the epithelial cell monolayer; and
(c) isolating the progenitor cells from the culture; (7) stimulating (C) the ex vivo proliferation of mammalian pancreatic beta-**islet cells**, comprising preparing a primary culture of mammalian pancreatic cells and contacting them with a cyclic AMP (cAMP) agonist to induce differentiation to beta-**islet cells**;
(8) stimulating (D) the ex vivo proliferation of **human** adult pancreatic beta cells comprising preparing a monolayer culture of primary **human** adult pancreatic cells and culturing the cells with a **growth factor** and a cAMP agonist to induce the primary culture to produce insulin-producing cells; (9) treating (E) a subject suffering from or at risk of developing, type 1 diabetes mellitus comprising: (a) preparing a primary culture of **human** adult pancreatic cells;
(b) contacting the culture with a reagent containing a cAMP agonist to induce the culture to produce insulin-producing cells; (c) harvesting the adult pancreatic cells; and (d) transplanting the cells of (c) in a subject; (10) producing, proliferating and differentiating (F) **human** adult pancreatic **islet cells** in clinically useful quantities comprising:
(a) seeding a bioreactor with a **human** pancreatic cell culture;
(b) perfusing the bioreactor with a complete growth medium supplemented with cAMP agonist to induce cells in the bioreactor to proliferate and differentiate into insulin-secreting cells; and (c) harvesting insulin-secreting cells from the bioreactor. ACTIVITY - Antidiabetic. Functional beta cells derived from the non-adherent portion of a differentiated pancreatic **duct** monolayer were implanted into streptozotocin (STZ)-treated diabetic mice. Insulin containing pellets were then implanted subcutaneously to stabilize the blood glucose and create a more stable environment for cell implantation. Within 48 hours of pellet implantation, the fasting blood glucose of the animals was reduced from 180 - 380 milligrams/deciliter blood glucose to less than 50 milligrams/deciliter. Cells were implanted under the renal capsule. An animal that received **duct**-derived cells showed a transient rescue of the diabetic state (4 - 5 day lowering of greater than 150 milligrams/deciliter blood glucose before rebounding to pre-implant blood glucose levels). MECHANISM OF ACTION - Insulin expression regulator. No biological data is given.
USE - Adult pancreatic cells that are isolated, proliferated, differentiated ex vivo and induced to produce insulin in vivo are used to treat a subject suffering from or at risk of developing, type 1 diabetes mellitus by transplanting the cells into the subject (claimed). The progenitor cells can be used in the treatment or prevention of a variety of pancreatic disorders, both exocrine and endocrine. Populations of differentiated pancreatic cells can be produced by the progenitor cells for repair subsequent to partial pancreatectomy (excision of a portion of the pancreas) or for regenerating or

replacing pancreatic tissue loss due to pancreatolysis e.g. destruction of pancreatic tissue. The progenitor cells and their progeny can be used to screen compounds for their ability to modulate growth, proliferation or differentiation of distinct progenitor cell populations from pancreatic **ductal** epithelial culture.
ADVANTAGE - The expansion and differentiation of a pancreatic stem/progenitor cell to create functional beta cells in **vitro** obviates the need for physical dissociation of tissue in order to obtain islets. The process has potential for greater reproducibility and control.

L33 ANSWER 10 OF 13 WPIDS COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-387772 [33] WPIDS
CROSS REFERENCE: 2000-387771; 2004-497131
DOC. NO. CPI: C2000-117776 [33]
TITLE: Low oxygen culturing of central nervous system progenitor cells useful in treatment of neurodegenerative disorders
DERWENT CLASS: B04; D16
INVENTOR: CESTE M; DOYLE J; MCKAY R; STUDER L; WOLD B J
PATENT ASSIGNEE: (CALY-C) CALIFORNIA INST OF TECHNOLOGY; (USSH-C) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 23

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC	
WO 2000029550	A2	20000525	(200033)*	EN	80[8]		<--
AU 2000021542	A	20000605	(200042)	EN			<--
EP 1131406	A2	20010912	(200155)	EN			<--
JP 2002530068	W	20020917	(200276)	JA	87		<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000029550	A2	WO 1999-US27613	19991118
EP 1131406	A2	EP 1999-965857	19991118
EP 1131406	A2	WO 1999-US27613	19991118
JP 2002530068	W	WO 1999-US27613	19991118
AU 2000021542	A	AU 2000-21542	19991118
JP 2002530068	W	JP 2000-582534	19991118

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000021542	A	Based on	WO 2000029550 A
EP 1131406	A2	Based on	WO 2000029550 A
JP 2002530068	W	Based on	WO 2000029550 A

PRIORITY APPLN. INFO: **US 1999-425462 19991022**
US 1998-195569 19981118
AN 2000-387772 [33] WPIDS
CR 2000-387771; 2004-497131
AB WO 2000029550 A2 UPAB: 20050410

NOVELTY - A method (I) for increasing **cell differentiation**, is new and comprises culturing undifferentiated central nervous system (CNS) cells in low ambient oxygen conditions, where the low ambient oxygen conditions promotes the **cellular differentiation** of the neuronal cells.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a method (II) for inhibiting apoptosis of a CNS cell in culture comprising growing the cell in low ambient oxygen conditions; (2) a method (III) for increasing the expansion of a CNS cell in culture comprising growing the cell in low ambient oxygen, where the cell exhibit increased expansion in the low ambient oxygen as compared to growing the cell in 20% oxygen incubator conditions; (3) a method (IV) for increasing cell proliferation in culture comprising growing CNS cells in low ambient oxygen, where the growth in low ambient oxygen increases cell proliferation compared to growing the cells in 20% oxygen incubator conditions; (4) a method (V) for preparing a cell for use against a neurodegenerative disorder comprising: obtaining a population of CNS cells; and growing the cells in low ambient oxygen conditions where the low ambient oxygen conditions increases the expression of a gene involved in the neurodegenerative disease; and (5) a cell (VI) produced according to the method comprising obtaining a starting CNS cell and growing the cell in low ambient oxygen conditions where the conditions produce a differentiated neuronal cell. ACTIVITY - Antiparkinsonian.
MECHANISM OF ACTION - Cell Transplantation Therapy.
USE - The methods may be used to prepare a cell for treatment of a neurodegenerative disorder, especially Parkinson's Disease. The cells have increased dopamine **production** and the methods promote cell survival, proliferation and/or **cellular differentiation** (all claimed). The cells are also amenable to cryopreservation and provide an accurate indication of how such cells behave biochemically in an in vivo setting. The methods can also provide cells that can be used in **vitro** to perform characterization studies or in vivo as replacement therapies for cells that have been damaged by disease, injury resulting from trauma, ischemia or a drug-induced injury. It is possible that the methods may be used to grow any cells routinely used in transplant therapies, including **islet cells** for diabetes, myoblasts for muscular dystrophy, and hepatocytes for liver disease.
ADVANTAGE - Under standard culture conditions, the ambient oxygen levels are distinctly hyperoxic and not at all within physiological ranges. The methods of the present invention promote proliferation and reduces apoptosis when cells are grown in lowered oxygen as compared to environmental oxygen conditions traditionally employed in cell culture techniques. Differentiation of precursor cells to specific fates is also enhanced in lowered oxygen, i.e. lowered oxygen is a useful adjunct for ex vivo generation of specific neuron types. DESCRIPTION OF DRAWINGS - The drawing shows the effect of lowered oxygen on precursor yield in **vitro** at varying plating densities.

L33 ANSWER 11 OF 13 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001045800 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10952464
TITLE: Modulation of rat pancreatic **acinoductal** transdifferentiation and expression of PDX-1 in **vitro**.
AUTHOR: Rooman I; Heremans Y; Heimberg H; Bouwens L
CORPORATE SOURCE: Department of Experimental Pathology, Free University of Brussels (VUB), Belgium.
SOURCE: Diabetologia, **(2000 Jul)** Vol. 43, No. 7, pp. 907-14.
Journal code: 0006777. ISSN: 0012-186X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 4 Dec 2000

AB AIMS/HYPOTHESIS: In adult pancreatic regeneration models exocrine acini are found to transdifferentiate to **duct**-like complexes. This has also been associated with the formation of new endocrine **islet cells**. We aimed to establish an in **vitro** model in which this transdifferentiation process is characterised and can be modulated. METHODS: Purified rat pancreatic acini were cultured in suspension. Differentiation was analysed by immunocytochemistry, electron microscopy, western blotting and RT-PCR. RESULTS: During culture acinar cells directly transdifferentiated without dividing, the cells lost their acinar phenotype and started to express cytokeratins 20 and 7 and fetal liver kinase-1 (Flk-1) receptors for vascular endothelial **growth factor**. Expression of the acinar pancreatic exocrine **transcription** factor (PTF-1) remained and the pancreatic duodenal homeobox-containing **transcription** factor (PDX-1) was induced. When transdifferentiation was completed, the cells started to express protein gene **product** 9.5, a panneuroendocrine marker. By combining these features, the transdifferentiated cells show similar characteristics to precursor cells during active beta-cell neogenesis. We were able to modulate the differentiation state by addition of nicotinamide or sodium butyrate, agents which are known to stimulate endocrine differentiation in other models. CONCLUSION/INTERPRETATION: Here, we present an in **vitro** system in which the **cellular differentiation** of putative pancreatic endocrine precursor cells and their PDX-1 expression can be modulated, thereby providing a possible model for the study of beta-**cell transdifferentiation**.

L33 ANSWER 12 OF 13 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999128119 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9930929
TITLE: Beta cell proliferation and **growth factors**.
AUTHOR: Nielsen J H; Svensson C; Galsgaard E D; Moldrup A; Billestrup N
CORPORATE SOURCE: Hagedorn Research Institute, Gentofte, Denmark.
SOURCE: Journal of molecular medicine (Berlin, Germany), **(1999 Jan)** Vol. 77, No. 1, pp. 62-6. Ref: 49
Journal code: 9504370. ISSN: 0946-2716.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 27 Aug 1999
Last Updated on STN: 27 Aug 1999
Entered Medline: 19 Aug 1999

AB Formation of new beta cells can take place by two pathways: replication of already differentiated beta cells or neogenesis from putative islet stem cells. Under physiological conditions both processes are most pronounced during the fetal and neonatal development of the pancreas. In adulthood little increase in the beta cell number seems to occur. In pregnancy, however, a marked hyperplasia of the beta cells is observed both in rodents and man. Increased mitotic activity has been seen both in vivo and in **vitro** in islets exposed to placental lactogen (PL), prolactin (PRL) and growth

hormone (GH). Receptors for both GH and PRL are expressed in **islet cells** and are upregulated during pregnancy. By mutational analysis we have identified different functional domains of the cytoplasmic part of the GH receptor. Thus the mitotic signaling only requires the membrane proximal part of the receptor and activation of the tyrosine kinase JAK2 and the **transcription** factors STAT1 and 3. The activation of the insulin gene however also requires the distal part of the receptor and activation of calcium uptake and STAT5. In order to identify putative autocrine **growth factors** or targets for **growth factors** we have cloned a novel GH/PRL stimulated rat **islet** gene **product** , Pref-1 (preadipocyte factor-1). This protein contains six **EGF** -like motifs and may play a role both in embryonic pancreas differentiation and in beta cell growth and function. In summary, the increasing knowledge about the mechanisms involved in beta **cell differentiation** and proliferation may lead to new ways of forming beta cells for treatment of diabetes in man.

L33 ANSWER 13 OF 13 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 97417253 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9272626
TITLE: Transient **transcriptional** activation of gastrin during sodium butyrate-induced differentiation of **islet cells**.
AUTHOR: Simon B; Merchant J L; Eissele R; Kohler K; Arnold R
CORPORATE SOURCE: Department of Internal Medicine, Philipps-University, Marburg, Germany.. simonb@mailer.uni-marburg.de
CONTRACT NUMBER: DK-45729 (NIDDK)
SOURCE: Regulatory peptides, **(1997 Jun 18)** Vol. 70, No. 2-3, pp. 143-8.
Journal code: 8100479. ISSN: 0167-0115.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 13 Oct 1997
Last Updated on STN: 29 Jan 1999
Entered Medline: 2 Oct 1997

AB Transient expression of pancreatic gastrin corresponds to a period of rapid **islet cell** development. After birth gastrin expression silencing is coincidental with **islet cell** terminal differentiation, while persistent expression is accompanied with nesidioblastosis and reexpression observed in **islet cell** tumors. Experiments with transgenic animals suggested that gastrin might act synergistically with **growth factors** to stimulate **islet cell** development. The present study intended to establish an in **vitro** cell culture model to analyse the molecular events controlling gastrin gene activation and repression dependent on **islet cell differentiation**. Sodium butyrate, a proliferation-arresting compound has previously been shown to differentiate insulinoma cells while increasing insulin **production**. The present paper demonstrates concomitant transient increase in gastrin mRNA, intracellular and secreted gastrin during sodium butyrate treatment. Increased gastrin expression was due to activation or derepression of gastrin promoter activity as revealed by promoter analyses. This in **vitro** model mimics the expression pattern of gastrin and insulin observed during fetal **islet cell** development and provides an excellent tool to analyse the molecular mechanisms controlling gastrin gene activation and selective repression during **islet cell differentiation**.

SEARCH HISTORY

```
=> d his ful

     (FILE 'HOME' ENTERED AT 16:07:33 ON 22 SEP 2007)

     FILE 'HCAPLUS' ENTERED AT 16:07:53 ON 22 SEP 2007
                E ROSENBERG LAWRENCE/AU
L1           147 SEA ABB=ON  ("ROSENBERG LAWRENCE"/AU OR "ROSENBERG LAWRENCE
                C"/AU OR "ROSENBERG LAWRENCE I"/AU OR "ROSENBERG LAWRENCE
                M"/AU OR "ROSENBERG LAWRENCE R"/AU)
L2            22 SEA ABB=ON  L1 AND ?NEOGENESIS?
L3             4 SEA ABB=ON  L2 AND ?ISLET?(W)CELL(W)?NEOGENESIS?
L4               ANALYZE L3 1-4 CT :       31 TERMS

     FILE 'REGISTRY' ENTERED AT 16:10:50 ON 22 SEP 2007
                E 3-D COLLAGEN/CN
                E DMEM F12/CN
L5             1 SEA ABB=ON  "DMEM/F 12"/CN

     FILE 'HCAPLUS' ENTERED AT 16:11:25 ON 22 SEP 2007
L6         25766 SEA ABB=ON  ?PANCREATIC?(W)?ISLET?(3W)?LANGERHANS? OR ?ISLET?(W
                )?CELL?
L7          2869 SEA ABB=ON  L6 AND ?TRANSCRIPT?
L8           403 SEA ABB=ON  L7 AND ?VITRO?
L9           127 SEA ABB=ON  L8 AND ?CELL?(W)?DIFFER?
L10           67 SEA ABB=ON  L9 AND ?DUCT?
L11           14 SEA ABB=ON  L9 AND ?DUCT?(4A)?ISLET?
L12            1 SEA ABB=ON  L10 AND ?POST?(W)?NATAL?
L13           67 SEA ABB=ON  L10 OR L11
L14            1 SEA ABB=ON  L13 AND (?POST?(W)?NATAL? OR ?CYSTIC?(W)?FORM?)
L15           23 SEA ABB=ON  L13 AND ?GROWTH?(W)?FACTOR?
L16            0 SEA ABB=ON  L13 AND 3(W)D(W)?COLLAGEN?
L17            0 SEA ABB=ON  L13 AND GEL(W)?MATRIX?
L18            4 SEA ABB=ON  L13 AND (L5 OR DMEM)
L19            4 SEA ABB=ON  L13 AND (L5 OR DMEM?)
L20           24 SEA ABB=ON  L15 OR L18 OR L19
L21            7 SEA ABB=ON  L20 AND (EGF OR ?CHOLERA?(W)?TOXIN?)
L22           24 SEA ABB=ON  L20 OR L21
L23           15 SEA ABB=ON  L22 AND ?HUMAN?
L24           24 SEA ABB=ON  L22 OR L23
L25           21 SEA ABB=ON  L24 AND (PRD<20051125 OR PD<20051125)

     FILE 'USPATFULL' ENTERED AT 16:18:53 ON 22 SEP 2007
L26         1841 SEA ABB=ON  L24 AND (PRD<20051125 OR PD<20051125)
L27         1568 SEA ABB=ON  L26 AND ?COLLAGEN?
L28          106 SEA ABB=ON  L27 AND GEL(W)?MATRIX?
L29           82 SEA ABB=ON  L28 AND (L5 OR DMEM)
L30            7 SEA ABB=ON  L29 AND ?CHOLERA?(W)?TOXIN?

     FILE 'HCAPLUS, USPATFULL' ENTERED AT 16:21:21 ON 22 SEP 2007
L31           28 DUP REMOV L25 L30 (0 DUPLICATES REMOVED)

     FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, WPIDS' ENTERED AT 16:21:38 ON 22
     SEP 2007
L32           19 SEA ABB=ON  L25
L33           13 DUP REMOV L32 (6 DUPLICATES REMOVED)

     FILE HOME
```

FILE HCAPLUS

FILE COVERS 1907 - 22 Sep 2007 VOL 147 ISS 14
FILE LAST UPDATED: 21 Sep 2007 (20070921/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 SEP 2007 HIGHEST RN 947723-94-6
DICTIONARY FILE UPDATES: 21 SEP 2007 HIGHEST RN 947723-94-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 20 Sep 2007 (20070920/PD)
FILE LAST UPDATED: 20 Sep 2007 (20070920/ED)
HIGHEST GRANTED PATENT NUMBER: US7272859
HIGHEST APPLICATION PUBLICATION NUMBER: US2007220648
CA INDEXING IS CURRENT THROUGH 20 Sep 2007 (20070920/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 20 Sep 2007 (20070920/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2007
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2007

FILE MEDLINE
FILE LAST UPDATED: 21 Sep 2007 (20070921/UP). FILE COVERS 1950 TO DATE.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS

FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 20 September 2007 (20070920/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE EMBASE
FILE COVERS 1974 TO 20 Sep 2007 (20070920/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE JAPIO
FILE LAST UPDATED: 10 SEP 2007 <20070910/UP>
FILE COVERS APRIL 1973 TO MAY 31, 2007

>>> GRAPHIC IMAGES AVAILABLE <<<

FILE WPIDS
FILE LAST UPDATED: 19 SEP 2007 <20070919/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200760 <200760/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> Now containing more than 1 million chemical structures in DCR <<<

>>> IPC Reform backfile reclassification has been loaded to 31 May 2007. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC and 20061231/UPIC and 20060601/UPIC. <<<

>>> Indian patent publication number format enhanced in DWPI - see NEWS <<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX PLEASE SEE
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<